

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



PCT

(43) International Publication Date
26 January 2006 (26.01.2006)

(10) International Publication Number
WO 2006/008526 A2

(51) International Patent Classification:
C12Q 1/68 (2006.01)

Caroline [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield Cheshire SK10 4TG (GB). MARSHALL, Gayle [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield Cheshire SK10 4TG (GB). SAM, Mehran [CA/US]; AstraZeneca R & D Boston, 35 Gatehouse Drive, Waltham, MA 02451 (US).

(21) International Application Number:
PCT/GB2005/002852

(74) Agent: GLOBAL INTELLECTUAL PROPERTY; AstraZeneca AB, SE-151 85 Södertälje (SE).

(22) International Filing Date: 20 July 2005 (20.07.2005)

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CY, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(30) Priority Data:
60/590,357 23 July 2004 (23.07.2004) US
60/619,027 18 October 2004 (18.10.2004) US

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(71) Applicant (*for AE, AG, AL, AM, AT, AU, AZ, BA, BB, BE, BF, BG, BJ, BR, BW, BY, BZ, CA, CF, CG, CH, CI, CM, CN, CO, CR, CU, CY, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FR, GA, GB, GD, GE, GH, GM, GN, GQ, GR, GW, HR, HU, ID, IE, IL, IN, IS, IT, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MC, MD, MK, ML, MN, MR, MW, MX, MZ, NA, NE, NG, NI, NL, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG only*): ASTRAZENECA AB [SE/SE]; SE-151 85 Södertälje (SE).

(71) Applicant (*for MG only*): ASTRAZENECA UK LIMITED [GB/GB]; 15 Stanhope Gate, London Greater London W1K 1LN (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): HUDSON, Kevin [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield Cheshire SK10 4TG (GB). SOUTH, Marie,

(54) Title: METHOD

(57) Abstract: The invention relates to a method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 or 2 as defined herein whereby to predict an increased likelihood of response to the erbB receptor drug. Preferred genes include any one of NES, GSPT2, ETR101, TAZ, CHST7, DNAJC3, NPAS2, PIN1, TCEA2, VAMP4, DAPK1, DAPK2, MLLT3, TNNC1, KIAA0931, ACOX2, EMP1, SLC20A1, SPRY2 or PGM1.

A2

WO 2006/008526 A2

METHOD

The present invention relates to sensitivity of tumours to therapeutic agents which can be predicted from the gene expression profile of the tumour and hence that the suitability of cancer patients for treatment with such therapeutic agents can be determined by measuring the relative expression levels of particular genes in tumour tissue.

The phosphorylation of proteins on tyrosine residues is a key element of signal transduction within cells. Enzymes capable of catalysing such reactions are termed tyrosine kinases. A number of these enzymes exist as integral components of transmembrane receptor molecules and are classified as receptor tyrosine kinases (RTKs). There are several members of this family of RTKs, class I of which includes the erbB family, e.g. epidermal growth factor receptor (EGFR), erbB2, erbB3 and erbB4. Binding of a variety of ligands to the external domain activates the EGFR tyrosine kinase domain. Activation causes EGFR itself and a number of cellular substrates to become phosphorylated on tyrosine residues. These phosphorylation reactions are a major component of growth factor induced proliferation of cells.

The erbB family of receptor tyrosine kinases are known to be frequently involved in driving the proliferation and survival of tumour cells (reviewed in Olayioye *et al.*, *EMBO J.*, 2000, **19**, 3159). One mechanism by which this can occur is over expression of the receptor at the protein level, for example as a result of gene amplification. This has been observed in many common human cancers (reviewed in Klapper *et al.*, *Adv. Cancer Res.*, 2000, **77**, 25) such as, non-small cell lung cancers (NSCLCs) including adenocarcinomas (Cerny *et al.*, *Brit. J. Cancer*, 1986, **54**, 265; Reubi *et al.*, *Int. J. Cancer*, 1990, **45**, 269; Rusch *et al.*, *Cancer Research*, 1993, **53**, 2379; Brabender *et al.*, *Clin. Cancer Res.*, 2001, **7**, 1850) as well as other cancers of the lung (Hendler *et al.*, *Cancer Cells*, 1989, **7**, 347).

It is now several decades since the study of retroviral mediated cellular transformation began to revolutionize our understanding of malignant transformation. Transformation was shown to be dependent on oncogenes carried by viruses and these were shown to have mammalian cellular counterparts, proto-oncogenes. In 1984, EGFR was described as the mammalian counterpart of the retroviral oncogene, v-erbB (Downward *et al.*). This, coupled to earlier observations describing a two component autocrine growth promoting mechanism in cancer cells consisting of EGF ligand and its receptor EGFR (Sporn & Todaro), strengthened

the hypothesis that EGFR signalling is an important contributor to tumourigenesis. Subsequent reports continued to provide evidence that EGFR is an attractive target for therapeutic intervention in Cancer (see Yarden & Sliwkowski for review). EGFR is markedly overexpressed across a large variety of epithelial Cancers (see Salomon et al) and some immunohistochemical studies have demonstrated EGFR expression is associated with poor prognosis. In addition to overexpression, it is recognised that there is potential for deregulated EGFR signalling in tumours via a number of alternative mechanisms including i) EGFR mutations ii) increased ligand expression and enhanced autocrine loop and iii) heterodimerisation and cross talk with other erbB receptor family members.

In addition, a wealth of pre-clinical information suggests that the erbB family of receptor tyrosine kinases are involved in cellular transformation. In addition to this, a number of pre-clinical studies have demonstrated that anti-proliferative effects can be induced by knocking out one or more erbB activities by small molecule inhibitors, dominant negatives or inhibitory antibodies (reviewed in Mendelsohn et al., Oncogene, 2000, 19, 6550).

Thus it has been recognised that inhibitors of these receptor tyrosine kinases should be of value as a selective inhibitor of mammalian cancer cells (Yaish et al. Science, 1988, 242, 933, Kolibaba et al, Biochimica et Biophysica Acta, 1997, 133, F217-F248; Al-Obeidi et al, 2000, Oncogene, 19, 5690-5701; Mendelsohn et al, 2000, Oncogene, 19, 6550-6565).

A number of small molecule inhibitors of erbB family of receptor tyrosine kinases are known, particularly inhibitors of EGF and erbB2 receptor tyrosine kinases. For example European Patent Application No. 0566226 and International Patent Applications WO 96/33980 and WO 97/30034 disclose that certain quinazoline derivatives which possess an anilino substituent at the 4-position possess EGFR tyrosine kinase inhibitory activity and are inhibitors of cancer tissue.

It has been disclosed by J R Woodburn et al. in Proc. Amer. Assoc. Cancer Research, 1997, 38, 633 and Pharmacol. Ther., 1999, 82, 241-250 that the compound N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine is a potent EGFR tyrosine kinase inhibitor. This compound is also known as Iressa (registered trade mark), gefitinib (United States Adopted Name), by way of the code number ZD1839 and Chemical Abstracts Registry Number 184475-35-2. The compound is principally identified hereinafter as gefitinib.

Gefitinib was developed as an inhibitor of epidermal growth factor receptor-tyrosine kinase (EGFR-TK), which blocks signalling pathways responsible for driving proliferation, invasion, and survival of cancer cells (Wakeling, A.E., et al. Cancer Res, 2002, 62(20), p5749). Gefitinib has provided clinical validation of small molecule inhibitors of EGFR. Potent anti-tumour effects as well as rapid improvements in NSCLC-related symptoms and quality of life have been observed in clinical studies that enrolled patients with advanced NSCLC who did not respond to platinum-based chemotherapy. The Phase II 'IDEAL' trials demonstrated that single agent gefitinib resulted in objective anti-tumour activity, symptomatic improvement and limited toxicity in patients with advanced NSCLC and previously treated with cytotoxic chemotherapy (Fukuoka et al., Kris et al). Objective response rate (Complete Response + Partial Response) was 18.4% and 11.8% respectively in the IDEAL 1 and IDEAL 2 trials. The differences in response in these clinical trials has been attributed to different population groups in the two trials, predominantly Japanese in IDEAL 1 and a predominantly European-derived population in IDEAL 2. Beyond objective responses, additional patients experienced stable disease and / or symptom improvement meaning that approximately 50% of patients overall benefit from gefitinib. The tumour response data has been the basis of initial regulatory approvals of gefitinib in advanced NSCLC in several markets.

It is important to be able to understand the basis of response to anti-cancer therapeutic agents such as gefitinib since this would allow clinicians to maximise the benefit/risk ratio for each patient, potentially via the development of diagnostic tests to identify patients most likely to benefit from gefitinib treatment. An obvious candidate marker of response to gefitinib has been EGFR expression level. However, gefitinib inhibition of growth of some cancer-derived cell lines and tumour xenografts is not well correlated with the level of expression of EGFR. Furthermore, studies alongside the IDEAL trials demonstrated that EGFR protein expression as measured by IHC was not an accurate predictor of response to gefitinib (Bailey et al). Although there are now several additional hypotheses based on genetics, genomics, proteomics, biochemical and other studies, there is still no pre-treatment predictive biomarker of gefitinib response currently approved by regulatory authorities. Possibly the most significant recent breakthrough in understanding gefitinib response has come from recent data (Lynch et al, Paez et al) indicating that mutation in the EGFR kinase domain predicts gefitinib hypersensitivity in NSCLC patients. Hypersensitivity is a vague term but in this field is generally understood to mean patients experiencing objective tumour responses (i.e. marked tumour regression,

normally above 50%). As well as demonstrating the EGFR mechanism of action for gefitinib, this may provide a basis for venturing into other disease settings such as first line, adjuvant and possibly earlier cancer intervention with EGFR inhibitors in a targeted subpopulation in NSCLC patients and other types of cancers carrying the EGFR mutation.

However, it is likely that restricting prescription of gefitinib to the mutant EGFR carrying tumour subgroup will deprive many patients who could benefit from gefitinib. Firstly there are emerging reports of gefitinib hypersensitive patients with undetectable EGFR mutation in their tumour and other patients with EGFR mutation who do not respond to gefitinib. Secondly, data reported at ASCO 2004 (Shepherd et al) indicated that the EGFR small molecule tyrosine kinase inhibitor erlotinib (Roche, Genentech, OSI) prolongs survival in advanced NSCLC previously treated with chemotherapy, by ~2 months across the population with resulting 41% reduction in risk of death at one year. Most interestingly, the survival benefit appears to be derived from patients in the stable disease response population as well as hypersensitive patients. This highlights the likely importance of identifying likely gefitinib responsive patients beyond those carrying EGFR mutation. Definitive survival benefit is also likely to be demonstrated from ongoing clinical trials with gefitinib.

The differential response of patients to chemotherapy treatments indicates that there is a need to find methods of predicting which treatment regimes best suit a particular patient.

There is an increasing body of evidence that suggests that patients' responses to numerous drugs may be related to a patients' genetic, genomic, proteomic, biochemical or profile and that determination of the genetic factors that influence, for example, response to a particular drug could be used to provide a patient with a personalised treatment regime. Such personalised treatment regimes offer the potential to maximise therapeutic benefit to the patient, whilst minimising, for example side effects that may be associated with alternative and less effective treatment regimes.

Therefore there is a need for methods that can predict a patients' response to a drug based on the results of a test that indicates whether the patient is likely to respond to treatment or to be resistant to treatment.

The present invention is based on the discovery that the sensitivity of tumours to therapeutic agents can be predicted from the gene expression profile of the tumour and hence that the suitability of tumour patients for treatment with such therapeutic agents can be determined by measuring the relative expression levels of particular genes in tumour tissue.

According to one aspect of the present invention there is provided a method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 as defined herein whereby to predict an increased likelihood of response to the erbB receptor drug.

According to another aspect of the present invention there is provided a method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 or DAPK2 whereby to predict an increased likelihood of response to the erbB receptor drug.

In one embodiment the method comprises testing a biological sample from the mammal for expression of any one of ACOX2, NPAS2, NES, CHST7, GSPT2, DAPK1, DAPK2 or TNNC1. More preferably the method comprises testing a biological sample from the mammal for expression of any one of NPAS2, NES, CHST7 or DAPK1. More preferably the method comprises testing a biological sample from the mammal for expression of at least two of NPAS2, NES, CHST7 or DAPK1. More preferably the method comprises testing a biological sample from the mammal for expression of at least three of NPAS2, NES, CHST7 or DAPK1. More preferably still the method comprises testing a biological sample from the mammal for expression of NPAS2, NES, CHST7 and DAPK1.

In an alternative embodiment the method comprises testing a biological sample from the mammal for expression of any one of NES, GSPT2, ETR101, TAZ, CHST7, DNAJC3, NPAS2, PIN1, TCEA2, VAMP4, DAPK1, DAPK2, MLLT3, TNNC1 or KIAA0931. More preferably the method comprises testing a biological sample from the mammal for expression of any one of DAPK1, DAPK2 or NES. More preferably the method comprises testing a biological sample from the mammal for expression of at least two of DAPK1, DAPK2 or NES. More preferably the method comprises testing a biological sample from the mammal for expression of DAPK1, DAPK2 and NES.

In a preferred embodiment the method additionally comprises testing a biological sample from the mammal for expression of any gene listed in Table 2 as defined herein. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1, SLC20A1, SPRY2 or PGM1. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

In an alternative preferred embodiment the method additionally comprises testing a biological sample from the mammal for expression of any gene listed in Table 2 as defined herein. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1, HCA127, UBL5, ZNF23, UROD, CD44, SPRY1, RAPGEF2, SLC20A1, NRP1, PGM1, SPRY2, PTGER3, SCN10A, KITLG, CDH1, HOP, BCL3 or OLFM1. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

Preferably the tumour is selected from the group consisting of leukaemia, multiple myeloma, lymphoma, bile duct, bone, bladder, brain, CNS, glioblastoma, breast, colorectal, cervical, endometrial, gastric, head, neck, hepatic, lung, muscle, neuronal, oesophageal, ovarian, pancreatic, pleural membrane, peritoneal membrane, prostate, renal, skin, testicular, thyroid, uterine and vulval. More preferably the tumour is selected from one of non-small cell lung, pancreatic, head or neck. More preferably the tumour is selected from one of non-small cell lung, head or neck.

Preferably the erbB receptor drug is selected from any one of gefitinib, erlotinib, PKI-166, EKB-569, HKI-272, lapatinib, canertinib, AEE788, XL647, BMS 5599626, cetuximab, matuzumab, panitumumab, MR1-1, IMC-11F8 or EGFR11. Most preferably the erbB receptor drug is gefitinib.

In a further preferred embodiment of the method of the invention the mammal is a human and the method comprises testing a biological sample from the human for increased expression of DAPK1 and decreased expression of NPAS2, NES, CHST7 or EMP1 whereby to predict an increased likelihood of response to gefitinib. In an alternative preferred embodiment of the method of the invention the mammal is a human and the method comprises testing a biological sample from the human for increased expression of DAPK1 and DAPK2 and decreased expression of NES and EMP1 whereby to predict an increased likelihood of response to gefitinib.

According to another aspect of the invention there is provided an isolated set of marker genes identified as having differential expression between tumour cells that are sensitive and resistant to an erbB receptor drug said gene set comprising one or more genes selected from at least the group consisting of the genes listed in Table 1 defined herein or DAPK2, including gene specific oligonucleotides derived from said genes. Preferably the set comprises at least 2

genes, more preferably at least 3 genes, more preferably at least 4 genes. More preferably the set comprises at least one gene selected from Table 2 as defined herein.

According to another aspect of the invention there is provided an isolated set of marker genes identified as having differential expression between tumour cells that are sensitive and resistant to an erbB receptor drug said gene set comprising one or more genes selected from at least the group consisting of the genes listed in Table 1 defined herein, including gene specific oligonucleotides derived from said genes. Preferably the set comprises at least 2 genes, more preferably at least 3 genes. More preferably the set comprises at least one gene selected from Table 2 as defined herein.

The present invention permits the improved selection of a patient, having or suspected of having a tumour, for treatment with an erbB receptor drug, in order to predict an increased likelihood of response to the erbB receptor drug.

In one embodiment, the method comprises testing a biological sample from the mammal for expression of at least one or more of the following from Table 1, which are found at lower levels in sensitive cells NPAS2, NES, CHST7, ACOX2 or GSPT2 or at least one or more of the following which are found at higher levels in sensitive cells DAPK1 or TNNC1. The Affymetrix ID and Affymetrix probe sequence for these genes are displayed in Table 1. In a preferred embodiment, the method further comprises testing a biological sample from the mammal for expression of DAPK2 which is found at higher levels in sensitive cells, whereby to predict an increased likelihood of response to the erbB receptor drug.

In an alternative embodiment, the method comprises testing a biological sample from the mammal for expression of at least one or more of the following from Table 1, which are found at lower levels in sensitive cells NES, GSPT2, ETR101, TAZ, CHST7, DNAJC3, NPAS2, PIN1, TCEA2 or VAMP4 or at least one or more of the following which are found at higher levels in sensitive cells DAPK1, DAPK2, MLLT3, TNNC1 or KIAA0931. The Affymetrix ID and Affymetrix probe sequence for these genes are displayed in Table 1.

In a preferred embodiment, the method further comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 2, whereby to predict an increased likelihood of response to the erbB receptor drug. In a preferred embodiment, the method comprises testing a biological sample from the mammal for expression of any one of the following genes listed in Table 2, which are found at lower levels in sensitive cells EMP1, SLC20A1, SPRY2 or PGM1, whereby to predict an increased likelihood of response to the

erbB receptor drug. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

In an alternative preferred embodiment, the method further comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 2, whereby to predict an increased likelihood of response to the erbB receptor drug. In a preferred embodiment, the method comprises testing a biological sample from the mammal for expression of any one of the following genes listed in Table 2, which are found at lower levels in sensitive cells EMP1, HCA127, UBL5, ZNF23, UROD, CD44, SPRY1, RAPGEF2, SLC20A1, NRP1, PGM1 or SPRY2 or at least one or more of the following which are found at higher levels in sensitive cells PTGER3, SCN10A, KITLG, CDH1, HOP, BCL3 or OLFM1 whereby to predict an increased likelihood of response to the erbB receptor drug. More preferably the method comprises testing a biological sample from the mammal for expression of EMP1.

In an especially preferred embodiment the method comprises testing a biological sample from the mammal for expression of NPAS2, NES, CHST7, DAPK1 and EMP1. High NPAS2, NES, CHST7 and EMP1 levels are associated with resistance to gefitinib and high DAPK1 levels are associated with sensitivity to gefitinib. Preferably, the assessment of expression comprises determination of whether DAPK1 levels are increased and NPAS2, NES, CHST7 and EMP1 levels are reduced.

In an alternative especially preferred embodiment the method comprises testing a biological sample from the mammal for expression of DAPK1, DAPK2, NES and EMP1. High EMP1 and NES levels are associated with resistance to gefitinib and high DAPK1 and DAPK2 levels are associated with sensitivity to gefitinib. Preferably, the assessment of expression comprises determination of whether DAPK1 and DAPK2 levels are increased and EMP1 and NES levels are reduced. In a most preferred embodiment the invention comprises determining the level of DAPK1 and EMP1.

According to another aspect of the invention there is provided a method for predicting clinical outcome of treatment with an erbB receptor drug for a mammal, having or suspected of having a tumour, comprising determining the level of any of the genes as described hereinabove in a biological sample taken from the tumour, or suspected tumour, wherein a poor outcome is predicted if:

- a) the expression level of DAPK1 is reduced; and /or

- b) the expression level of NPAS2, NES, CHST7 and EMP1 is increased.

According to another aspect of the invention there is provided a method for classifying cancer comprising, determining the level of any of the genes as described hereinabove in a biological sample taken from a tumour, or suspected tumour, wherein tumours expressing elevated levels of DAPK1 and / or reduced levels of NPAS2, NES, CHST7 or EMP1 are predicted as sensitive to treatment with erbB receptor drugs.

According to another aspect of the invention there is provided a method for predicting clinical outcome of treatment with an erbB receptor drug for a mammal, having or suspected of having a tumour, comprising determining the level of any of the genes as described hereinabove in a biological sample taken from the tumour, or suspected tumour, wherein a poor outcome is predicted if:

- a) the expression level of DAPK1 or DAPK2 is reduced; and /or
- b) the expression level of EMP1 or NES is increased.

According to another aspect of the invention there is provided a method for classifying cancer comprising, determining the level of any of the genes as described hereinabove in a biological sample taken from a tumour, or suspected tumour, wherein tumours expressing elevated levels of DAPK1 or DAPK2 and / or reduced levels of EMP1 or NES are predicted as sensitive to treatment with erbB receptor drugs.

According to another aspect of the invention there is provided a method for treating a disease condition in a mammal having, or suspected of having, a tumour, predicted to be resistant or non responsive to erbB receptor drug treatment based on the level of any of the genes as described hereinabove, comprising: providing a resistance-surmounting quantity of an erbB receptor drug and administering the resistance-surmounting quantity of the erbB receptor drug to the mammal.

In a preferred embodiment the mammal is a primate. In a most preferred embodiment the mammal is a human. In a preferred embodiment the patient is a primate. In a most preferred embodiment the patient is a human.

The term "erbB receptor drug" includes drugs acting upon the erbB family of receptor tyrosine kinases, which include EGFR, erbB2 (HER), erbB3 and erbB4 as described in the background to the invention above. In a preferred embodiment the erbB receptor drug is an erbB receptor tyrosine kinase inhibitor. In a preferred embodiment the erbB receptor drug is an EGFR tyrosine kinase inhibitor.

In a more preferred embodiment the EGF receptor tyrosine kinase inhibitor is selected from gefitinib, Erlotinib (OSI-774, CP-358774), PKI-166, EKB-569, HKI-272 (WAY-177820), lapatinib (GW2016, GW-572016), canertinib (CI-1033, PD183805), AEE788, XL647, BMS 5599626 or any of the compounds as disclosed in WO03/082831, WO05/012290, WO05/026157, WO05/026150, WO05/026156, WO05/028470, WO05/028469, WO2004/006846, WO03082831, WO03/082290 or PCT/GB2005/000237.

In another preferred embodiment the erbB receptor drug is an anti-EGFR antibody such as for example one of cetuximab (C225), matuzumab (EMD-72000), panitumumab (ABX-EGF/rHuMAb-EGFr), MR1-1, IMC-11F8 or EGFR-L11.

We contemplate that erbB receptor drugs may be used as monotherapy or in combination with other drugs of the same or different classes. In an especially preferred embodiment the EGF receptor tyrosine kinase inhibitor is gefitinib.

In a preferred embodiment the present invention is particularly suitable for use in predicting the response to the erbB receptor drug as described hereinbefore in those patients or patient population with a tumour which is dependent alone, or in part, on an erbB tyrosine kinase receptor. Such tumours include, for example, non-solid tumours such as leukaemia, multiple myeloma or lymphoma, and also solid tumours, for example bile duct, bone, bladder, brain/CNS, glioblastoma, breast, colorectal, cervical, endometrial, gastric, head and neck, hepatic, lung, muscle, neuronal, oesophageal, ovarian, pancreatic, pleural/peritoneal membranes, prostate, renal, skin, testicular, thyroid, uterine and vulval tumours.

In a preferred embodiment the present invention is particularly suitable for identifying a patient with head, neck, pancreatic, glioblastoma, colorectal or breast tumour for drug treatment. In an especially preferred embodiment the present invention also is particularly suitable for identifying those patients with NSCLC, more particularly advanced NSCLC including advanced adenocarcinoma that will respond to treatment with an erbB receptor drug as hereinbefore defined.

The present invention provides advantage in the treatment of tumours such as NSCLC, especially advanced NSCLC by identifying "individual cancer profiles" of NSCLC and so determining which tumours would respond to erbB receptor drug such as gefitinib.

The present invention is particularly useful in the treatment of patients with advanced NSCLC who have failed previous chemotherapy, such as platinum-based chemotherapy. The present invention is also particularly useful in the treatment of patients with locally advanced

(stage IIIB) or metastasized (stage IV) NSCLC who have received previous chemotherapy, such as platinum-based chemotherapy. The present invention is also useful in adjuvant therapy or as a first-line therapy.

In a preferred embodiment there is provided a method of selecting a human, having or suspected of having a tumour, for treatment with gefitinib which comprises testing a biological sample, from the mammal for expression of NPAS2, NES, CHST7, DAPK1 and EMP1, whereby to predict an increased likelihood of response to gefitinib.

In a preferred embodiment there is provided a method of selecting a human, having or suspected of having a tumour, for treatment with gefitinib which comprises testing a biological sample, from the mammal for expression of DAPK1, DAPK2, NES and EMP1 whereby to predict an increased likelihood of response to gefitinib.

According to another aspect of the invention there is provided a method of predicting the responsiveness of a patient or patient population with cancer, for example lung cancer, to treatment with chemotherapeutic agents, especially erbB receptor drugs, comprising comparing the differential expression of any of the genes described herein.

In one embodiment the assessment of expression is performed by gene expression profiling using oligonucleotide-based arrays or cDNA-based arrays of any type, particularly where large numbers of genes are analysed simultaneously. In an alternative embodiment, RT-PCR (reverse transcription- Polymerase Chain Reaction), real-time PCR, *in-situ* hybridisation, Northern blotting, Serial analysis of gene expression (SAGE) for example as described by Velculescu et al Science 270 (5235): 484-487, or differential display or any other method of measuring gene expression at the RNA level could be used. Details of these and other general molecular biology techniques can be found in Current Protocols in Molecular Biology Volumes 1-3, edited by F M Asubel, R Brent and R E Kingston; published by John Wiley, 1998 and Sambrook, J. and Russell, D.W., Molecular Cloning: A Laboratory Manual, the third edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 2001.

In another embodiment the assessment of expression is performed by measurement of protein levels encoded by the aforementioned genes. For example, an immunohistochemistry-based assay or application of an alternative proteomics methodology.

In another embodiment the assessment of expression is performed by measurement of activity of the proteins encoded by the aforementioned genes, for example in a bioassay.

In a preferred embodiment the biological sample would have been obtained using a

minimally invasive technique to obtain a small sample of tumour, or suspected tumour, from which to determine gene expression profile. Such techniques include, for example tumour biopsy, such as transbronchial biopsy. The profile of gene expression of transbronchial biopsy specimens whose size is about 1 mm may be measured for example using a suitable amplification procedure.

Another aspect of the invention provides a kit for use in a method of predicting the responsiveness of a patient or patient population with a tumour, to treatment with chemotherapeutic agents, especially erbB receptor drugs, comprising a means for measuring the levels of any of the genes as described hereinabove. Preferably the genes are attached to a support material or membrane such as nitrocellulose, or nylon or a plastic film or slide.

In a further preferred embodiment the present invention includes administration of an erbB receptor drug to a mammal selected according the methods described hereinabove.

According to another aspect of the invention there is provided a method of using the results of the methods described above in determining an appropriate dosage of an erbB receptor drug.

In a preferred embodiment the biological sample comprises either a single sample which may be tested for expression of any of the genes as described hereinabove, or multiple samples which may be tested for expression of one or more of the genes as described hereinabove.

The invention is illustrated by the following non-limiting examples in which:

Fig 1 illustrates a xenograft (A549 cell line) which when grown as a xenograft in athymic mice is sensitive to gefitinib. This involved oral dosing, once daily, at the dose indicated. Y axis = mean tumour volume in cm³; x axis = days after treatment.

Fig 2 illustrates a xenograft (MKN45 cell line) which when grown as a xenograft in athymic mice is resistant to gefitinib. This involved oral dosing, once daily, at the dose indicated. Y axis = mean tumour volume in cm³; x axis = days after treatment.

Figures 3, 4, 5 and 6 show examples of specific gene expression profiled across a wider panel of gefitinib sensitive and resistant lines, where definition of sensitivity is based on response to gefitinib when grown as a xenograft, to increase confidence that the expression profile of each gene is truly predictive. Iressa sensitivity is based on xenografts data. The cell lines and the tumours from which they are derived are as follows; KB – head and neck, HT29 - colon, BT474 – breast, DU145 – prostate, LoVo – colon, MCF7 – breast, GEO – colon, A549 – lung,

A431 - epidermoid, H322 – lung, HX147 – lung, RT112 – bladder, MiaPaCa2 – pancreas,

MKN45 – gastric, MDAMB231 – breast, PC3 - prostate, Calu6 – lung, SW620 – colon.

The legend key is S=sensitive, U=unknown and R=resistant.

Fig 3 shows EMP1 basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Fig 4 shows DAPK1 basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Fig 5 shows DAPK2 basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Fig 6 shows NES basal expression in Cell Culture - wider cell panel (Taqman RT-PCR).

Example 1**Gene Expression in Gefitinib Resistant or Sensitive Tumour Cell Lines – Cell Culture and Xenograft Studies**

We identified genes useful to predict response to erbB receptor drugs in the clinic. This is based on studies with gefitinib, but the findings are applicable to erbB receptor drugs in general.

The gene lists have been assembled by comparing tumour cell lines which have been demonstrated to be either sensitive to gefitinib or resistant to gefitinib. This definition is based on the response observed when the tumour cell line is implanted into nude mice and grown as a xenograft. This definition has been used for all the pre-clinical studies described herein.

Initially a small panel of six human tumour cell lines were assembled, three which are sensitive to gefitinib and three which are resistant to gefitinib in the xenograft setting defined above.

The sensitive cell lines were;

1. Lovo (ATCC¹ No. CCL-229) – colon tumour cell line
2. KB (ATCC No. CCL-17) – initially reported as a nasopharyngeal cell line (although more recently reported as Hela derived (cervical carcinoma)
3. HT29 (ATCC No. HTB-38) – colon tumour cell line

The resistant cell lines were;

1. MKN 45 (source - Nottingham University, UK) – gastric tumour cell line
2. Calu 6 (ATCC No. HTB-56) – lung tumour cell line
3. PC3 (ATCC No. CRL-1435) – prostate tumour cell line

¹ATCC = American Type Culture Collection

The cell lines were grown both in cell culture and as xenografts, RNA prepared and the basal expression profiles determined by measuring RNA expression on the Affymetrix microarray platform. As part of our studies, the term ‘basal’ has been used to indicate constitutive or steady state expression levels (rather than expression levels which are modulated as a consequence of administration of an erbB ligand or gefitinib to the cells). Figure 1 illustrates the sensitivity of A549 xenografts (used in Example 3 below) to treatment with gefitinib. Figure 2 illustrates the resistance of MKN45 xenografts to gefitinib. See Example 2 below for analysis of results.

Example 2**Statistical analyses of cell culture and xenograft data sets**

The following statistical analyses were performed separately for cell culture and xenograft data sets. Probe sets were eliminated if their signal was not distinguishable from background noise across all RNA samples in the set. Mixed ANOVA (see for example Scheffe, 1959) was applied separately to each remaining probe set to generate p values. The p values were then used to calculate Q values (Storey). The Q values indicate the expected proportion of genes in a gene list which are not truly differentially expressed but have been falsely discovered (False Discovery Rate or FDR). Q value cut-offs appropriate in the different studies were identified and applied, based on graphical examination of the p value and Q value results, in conjunction with fold change. The final genelists for each study were generated using Q value and fold change (FC) cut-offs. The different genelists were then combined to display an overall list of genes which showed consistent differences in expression profiles between the cell lines in the sensitive and resistant groups.

Further details of the analysis procedures are provided as follows. Fold change (FC) was calculated based on the mean of sensitive cells divided by the mean of resistant cells. To generate gene lists, FC cut-off of two-fold (2X) change in either direction was used in all cases. Furthermore FDR Q values were used to narrow down the lists and obtain the most significant gene changes across sensitive versus resistant cell lines. In the case of cell culture, Q value cut-off is 0.3. In the case of xenograft, Q value cut-off is 0.6. The different cut-offs used reflect the different design and variance values associated with each experiment.

In cell culture studies, lists were obtained based on the above criteria for cells grown either in full serum containing medium or in charcoal stripped serum. In the xenograft study, the same as above was performed for separate sets of tumours harvested at 18hr intervals. Gene lists contain some redundancy in genes where appropriate to illustrate consistency of results obtained for example with different probe sets.

Example 3**Identification of predictive genes**

Genes which have not previously been identified as predictive of erbB receptor drug sensitivity are listed in Table 1. Other genes which we have identified to be optionally used in combination with Table 1 genes are listed in Table 2.

Key to Tables:

‘Affymetrix ID’ – the Affymetrix probe set identifier

‘Sequence’ – target sequence relating to the Affymetrix probe set indicated by ‘Affymetrix ID’

“+ if up in sensitive” means that the gene is relatively highly expressed in sensitive cells. (Consequently, absence of a “+” means that the gene is relatively highly expressed in resistant cells).

‘Gene Title’ - The current annotation of the gene relating to ‘Affymetrix ID’ based on UniGene 133

‘Gene Symbol’ – shorthand synonym for the gene title

‘Locus Link’ & RefSeq Transcript ID’ are provided for gene identification purposes.

Combining genes has the potential to generate an improved diagnostic over genes used in isolation. Collective gene expression profiles (at the RNA and/ or protein level) may be more likely to identify patients most likely to benefit from gefitinib rather than the expression level of one gene in isolation.

It may be more practical when developing a pre-treatment response prediction diagnostic to work with a truncated gene list from tables 1 and / or 2. A number of criteria have been used to shorten the gene list to identify those genes which are most predictive of response. Firstly the statistical (p values and Q values or FDR values) can indicate the statistical significance of a gene.

Secondly, the differential expression (fold change) between the sensitive and resistant groups indicates the potential sensitivity of a marker to be used in a diagnostic test (highest fold change between sensitive group and resistant group is preferred).

Thirdly, we have performed RT-PCR based expression profiling across a wider panel of gefitinib sensitive and resistant human tumour cell lines to increase confidence that the expression profile of each gene is truly predictive. Figs 3, 4, 5 and 6 show examples of specific gene expression profiled across a wider panel of cell lines as set out below.

The sensitive human tumour cell lines, where definition of sensitivity is based on response to Iressa when grown as a xenograft:

- a. BT474 (ATCC No. HTB-20) – breast tumour cell line
- b. DU145 (ATCC No. HTB-81) – colon tumour cell line

- c. MCF7 (ATCC No. HTB-22, sourced from ICRF (now CR-UK), London), - breast tumour cell line
- d. GEO colon tumour cell line. RNA obtained from Fortunato Ciardiello, Cattedra di Oncologia Medica, Dipartimento Medico-Chirurgico di Internistica Clinica e Sperimentale "F. Magrassi e A. Lanzara," Seconda Universita delgi Studi di Napoli, Via S. Pansini, 5-80131, Naples, Italy.
- e. A549 (ATCC No. CCL-185) – lung tumour cell line
- f. A431 (ATCC No. CRL-155) – epidermoid cell line

The resistant human tumour cell lines, where definition of sensitivity is based on response to Iressa when grown as a xenograft:

- 1) HX147 - (source: ICRF (now CR-UK), London) – lung tumour cell line
- 2) RT112 - bladder tumour cell line (DSMZ No ACC 418)
- 3) MiaPac2 (ECACC 85062806, ref. no. 001611) pancreatic tumour cell line
- 4) MDAMB231 (ATCC No. HTB-26) – breast tumour cell line
- 5) SW620 (ECACC CCL-227) – colon tumour cell line

ATCC = American Type Culture Collection

DSMZ - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (German Collection of Micro-organisms and Cell Cultures)

ECACC = European Collection of Cell Cultures

In isolation, each of these genes is reasonably predictive of gefitinib response, but collectively they can be applied to make predictions with a higher level of confidence.

The Affymetrix probe sets identifiers for the genes in the above diagnostic genelists are indicated in Tables 1 and 2. Current Affy IDs are based on Affy U133 chipset. For the avoidance of doubt, the target sequences of the Affymetrix probe sets which identified the listed genes are also provided in Tables 1 and 2.

Without wishing to be bound by theoretical considerations, it is contemplated that the specific sequences used to detect target genes in the Examples may define specific splice variants or sequences in homologous genes. Therefore in one embodiment, a listed gene for use in the method of the invention is defined by the specific sequence used in said Examples. In another embodiment, a gene for use in the method of the invention is not limited by the specific sequence used in these Examples. Indeed the fact that some genes in Tables 1 and 2 have been identified using different sequences (gene “redundancy”) and confirmatory RT-PCR studies (see

Example 4) provides evidence that usefulness in the method of the invention is not generally limited to the specific sequences used to measure the target gene.

Note, in the event of a discrepancy in the sequence between Tables 1 and 2 and the Sequence Listing, the sequence as provided in the Tables is preferred.

Table 1: as described in priority application US60/619027 filed on 18/10/2004.

PEX3	peroxisomal biogenesis factor 3	203972_s_at		SEQ ID NO:42	
	protein (peptidyl-prolyl cis/trans isomerase) NIMA-interacting 1 / protein (peptidyl-prolyl cis/trans isomerase) NIMA-interacting 1	202927_at		SEQ ID NO:43	
PRKCA	"protein kinase C, alpha"	213093_at		SEQ ID NO:44	
RIOK3	RIO kinase 3 (yeast)	202129_s_at		SEQ ID NO:45	

Table 2: as described in priority application US60/619027 filed on 18/10/2004.

FLJ22662	hypothetical protein FLJ22662	218454_at	+	79887 NM_024829
GADD45 B	"growth arrest and DNA-damage-inducible, beta / growth arrest and DNA-damage-inducible, beta"	207574_S_at		4616 NM_015675
HIF1A	"hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor) / hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)"	200989_at		3091 NM_001530 / NM_181054
HOP	homeodomain-only protein / homeodomain-only protein	211597_S_at	+	84525 NM_082495 / NM_139211 / NM_139212
HOXC10	homeo box C10 / homeo box C10	218959_at		3226 NM_017409

ITGB2	"integrin, beta 2 (antigen CD18 (p95), lymphocyte function-associated antigen 1; macrophage antigen 1; integrin, beta 2 (antigen CD18 (p95), lymphocyte function-associated antigen 1; macrophage antigen 1 (mac-1) beta subunit)"	202803_s_at	3689	NM_000211 SEQ ID NO:94
KHDRBS 3	"KH domain containing, RNA binding, signal transduction associated 3 / KH domain containing, RNA binding, signal transduction associated 3"	209781_s_at	10656	NM_006558 SEQ ID NO:95
KRT13	keratin 13 / keratin 13	207935_s_at	+	NM_002274 / NM_153490 SEQ ID NO:96
LASS6	LAG1 (longevity assurance homolog 6 (<i>S. cerevisiae</i>)	212446_s_at	+	NM_203463 SEQ ID NO:97

RRM1	ribonucleotide reductase M1 polypeptide	201476_s_at	+	SEQ ID NO:119	6240	NM_001033
SEMA3B	"sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B / sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B"	203071_at	+	SEQ ID NO:120	7869	NM_004636
SERPIN E ₁	"serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1"	202627_s_at		SEQ ID NO:121	5054	NM_000602
SERPIN E ₁	"serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1"	202628_s_at		SEQ ID NO:122	5054	NM_000602
SLC20A1	"solute carrier family 20 (phosphate transporter), member 1 / solute carrier family 20 (phosphate transporter), member 1"	201920_at		SEQ ID NO:123	6574	NM_005415

TIMP3	"tissue inhibitor of metalloproteinase 3 (Sorbsy fundus dystrophy, pseudoinflammation)"	201150_s_at		7078	NM_000362	SEQ ID NO:134
TNFRSF6	"tumor necrosis factor receptor superfamily, member 6"		+	355	NM_00043 / NM_152871 / NM_152872 / NM_152873 / NM_152874 / NM_152875 / NM_152876 / NM_152877	SEQ ID NO:135
TNFRSF6	"tumor necrosis factor receptor superfamily, member 6"	204781_s_at		355	NM_00043 / NM_152871 / NM_152872 / NM_152873 / NM_152874 / NM_152875 / NM_152876 / NM_152877	SEQ ID NO:136
TNFSF10	"tumor necrosis factor (ligand) superfamily, member 10"	215719_x_at	+	8743	NM_003810	SEQ ID NO:137
TNFSF10	"tumor necrosis factor (ligand) superfamily, member 10 / tumor necrosis factor (ligand) superfamily, member 10"	202687_s_at	+	8743	NM_003810	SEQ ID NO:138

Example 4**RT-PCR Confirmation Studies**

In addition, the sequence of the RT-PCR primers used in the confirmatory follow up studies as highlighted in Figs 3, 4, 5 and 6 are listed in Table 3. Note that DAPK2 was not identified by Affymetrix analysis, only via follow up of the DAPK gene family by RT-PCR following discovery of predictivity of DAPK1. Hence no Affymetrix ID or Affymetrix ID sequence is provided for DAPK2.

Table 3

Sequences relevant to genes followed up by RT-PCR (see Figs 3, 4, 5 & 6)

(all sequences written 5'-3')

Gene	affy id	affy probe seq	Taqman Forward Primer	Taqman Reverse Primer	Taqman probe
EMP1	201324_at	CACCAAATTACCTAGGCTGAGGTAGAGAGATTGCCAGCAAA AACTGTGGGAAGATGAACCTTGTCAATTGATTCAATTATCAC ATGATTATAGAAGGCTGTCTAGTGCAAAAAACATCTACATT TCAGACATATCCAAGGGAATACTCACATTGGTTAAGAAGTT GAACATGACTGGAGTAACCATGTATTCCCTTATCTTTACTT TTTCTGTGACATTATGTGCTCATGTAATTGCAATTACTCG GTGGATTGTCTAGTACTGTATTGGCTCTTCGTTAAT	AGCCATCCTG CCCTCTGA	ACCTTACAAC TCTCTTCC	CAAAGCA AAACATC ACATTCC AGTC
NES	218678_at	GCAGCACTTAACTTACGATCTTGACATA CGGTTCTGGC TGAGAGGCCCTGGCCCGCTAAGGTGAAAAGGGGTGGGCAA AGGAGCTACTCCAAGAACATGGAGGCTGTAGGAATATAAACCTC CCACCCCTGCAAAGGGAACTCTCTGCTGCTCCATTCTCATAGG CTAAGTCAGCTGAATCCGATAGTACTAGGTCCCCCTCCCTCC GCATCCCGTAGCTGAAAAGGCCCTGGGCCAGAGGCTTC TCCAAAGGGAGGGTGACATGCTGGCTTTGTGCCCAAGCTCA CCAGCCCTGCCACCTCACTGCAAGTAGTQACCATCTCAC TGCAGTAGCACGCCCTCTGGGCCCTGGCTGTGGCTTAAT GGAGGTGACGGCACTCCCATTGTGCTGACTCCCCCATCCCT GCCACGCTGTGGCCCTGCCTGGCTAGTCCCTGCCTGAATAAA G	GCCCCCTTCA GGAGGAGGA	AGTGCGGGGG AGATGGTCTT	AGTGCTC TGAAGAC CTCTTGG GC
DAPK1	203139_at	CCTCCCTCCAGGGTGATTTATGATCAGTGTGCTCTAGGA AGACATTTCGCCCTTGCTTTGTCAATGTCATGGTGAAAG TCCACATGAAACCTACACACTGTCACTGCTTCATCATCCCTCTC ATCTCAGGTAGAAGGTTGACACAGTTGTAAGGGTACAGAGAC CTATGTAAGAACCTCAGAAGAGCCCTGACTCATCTTGTGGCA GTCCCTATAATTGGTGACATAGCCAGATGGTTCCACATTAG ATCCTGGTTCTACACTCCCTGACTTGTGAAAGTCTAAAGCAGAA AATAAAGGAAGCAAGTTTCTCCATGATTTAAATTGTGATC GAGTTTAAATTGATAGGAGGGAACATGTCTTAATTCTCTGT CCTGAGAA	AGGAAACGCT ACCTCTCTGT	CTGGAGGAAGG ATTCCCTCT	CTTGCTG TATGCTG ATCATCG CC
DAPK2	Not applicable	Not applicable	GGGTAGGCAC CTGGCATIC	AGTGCAGTGG CGTGATCTC	TACTCCA GGGGCT GAGGTGA CA

Example 5**Diagnostic test for Clinical Studies**

The predictive gene lists above have been generated using the preclinical studies described. The following approach is employed to develop a diagnostic test for the clinical setting based on this data.

- a) Identify patients which represent the population of individuals whom we would expect to derive benefit from a diagnostic test, and for which pre-treatment tumour samples and outcome of gefitinib treatment are known or will be available. For each sample the expression level for our genes of interest is evaluated, using for example the RNA signal from RT-PCR. QC procedures are applied to identify the set of samples and genes to take forward to step b).
 - a) Identify a subset of the genes which together are able to distinguish between patients showing different responses to gefitinib. There are a variety of methods which are useful to select the subset of genes and combine their expression values to provide a prediction, possibly a predictive value and a corresponding threshold which distinguishes between different patient groups. An example is stepwise Linear Discriminant Analysis where genes that distinguish well between patient groups are successively added to a linear combination until addition of a further gene does not provide additional predictive power (Mardia et al.). The threshold value of the linear combination is then selected to give the appropriate sensitivity and specificity properties.
 - d) Tool validation would partly be carried out during development in step 2, for example using cross validation and permutation tests. In addition, the finally developed diagnostic procedure (gene subset and method of combining to generate a prediction and a platform for biological analysis) is tested and validated in its entirety using an independent set of samples not used within tool development in step b).

References

- Bailey et al Lung Cancer (2003) 41 S2 , S71
Downward et al. (1984) Nature, 307, p521
Fukuoka et al (2003) J. Clin. Oncol., 21, p2237
Kris et al. (2003) JAMA, 290, p2149
Lynch et al.(2004) New England Journal of Medicine, 350(21) p2129

- Mardia K.V., Kent J.T., Bibby J.M. (1979) "Multivariate Analysis" London, Academic Press Inc. Ltd.
- Paez et al. (2004) Science, 304 p
- Salomon et al. (1995) Crit. Rev. Oncol. Haematol, 19, p183
- Scheffe, H. (1959) "The Analysis of Variance" New York, Wiley
- Sporn & Todaro (1980) New England Journal of Medicine 303, p878
- Storey (2003) "Statistical Significance for Genome Wide Studies" PNAS, vol 100, issue 16, pp 9440 – 9445
- Yarden & Sliwkowski (2001) Nature Reviews Molecular Cell Biology, 2, p127

CLAIMS

1. A method of selecting a mammal having or suspected of having a tumour for treatment with an erbB receptor drug which comprises testing a biological sample from the mammal for expression of any one of the genes listed in Table 1 or DAPK2, whereby to predict an increased likelihood of response to the erbB receptor drug.
2. A method according to claim 1 comprising testing a biological sample from the mammal for expression of any one of NPAS2, NES, CHST7, DAPK1, ACOX2, GSPT2, TNNC1 or DAPK2.
3. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of any one of NPAS2, NES, CHST7 or DAPK1.
4. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of at least two of NPAS2, NES, CHST7 or DAPK1.
5. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of at least three of NPAS2, NES, CHST7 or DAPK1.
6. A method according to any preceding claim comprising testing a biological sample from the mammal for expression of NPAS2, NES, CHST7 and DAPK1.
7. A method according to any preceding claims additionally comprising testing a biological sample from the mammal for expression of any gene listed in Table 2 as defined herein.
8. A method according to claim 7 comprising testing a biological sample from the mammal for expression of any one of EMP1, SLC20A1, SPRY2 or PGM1.
9. A method according to any one of claims 7-8 comprising testing a biological sample from the mammal for expression of EMP1.

10. A method according to any preceding claim wherein the tumour is selected from the group consisting of leukaemia, multiple myeloma, lymphoma, bile duct, bone, bladder, brain, CNS, glioblastoma, breast, colorectal, cervical, endometrial, gastric, head, neck, hepatic, lung, muscle, neuronal, oesophageal, ovarian, pancreatic, pleural membrane, peritoneal membrane, prostate, renal, skin, testicular, thyroid, uterine and vulval.
11. A method according to claim 10 wherein the tumour is selected from one of non-small cell lung, pancreatic, head or neck.
12. A method according to any preceding claim wherein the erbB receptor drug is selected from any one of gefitinib, erlotinib, PKI-166, EKB-569, HKI-272, lapatinib, canertinib, AEE788, XL647, BMS 5599626, cetuximab, matuzumab, panitumumab, MR1-1, IMC-11F8 or EGFR-L11.
13. A method according to claim 12 wherein the erbB receptor drug is gefitinib.
14. A method according to any preceding claim wherein the mammal is a human and in which the method comprises testing a biological sample from the human for increased expression of DAPK1 and decreased expression of NPAS2, NES, CHST7 and EMP1 whereby to predict an increased likelihood of response to gefitinib.

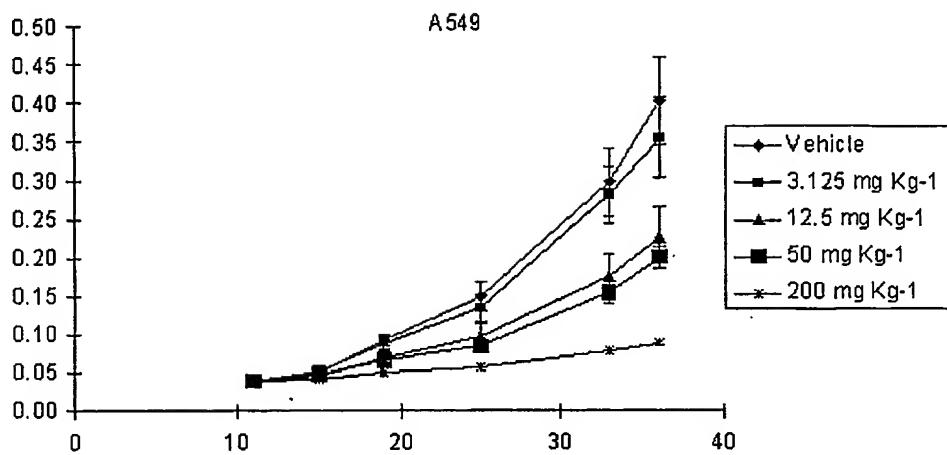
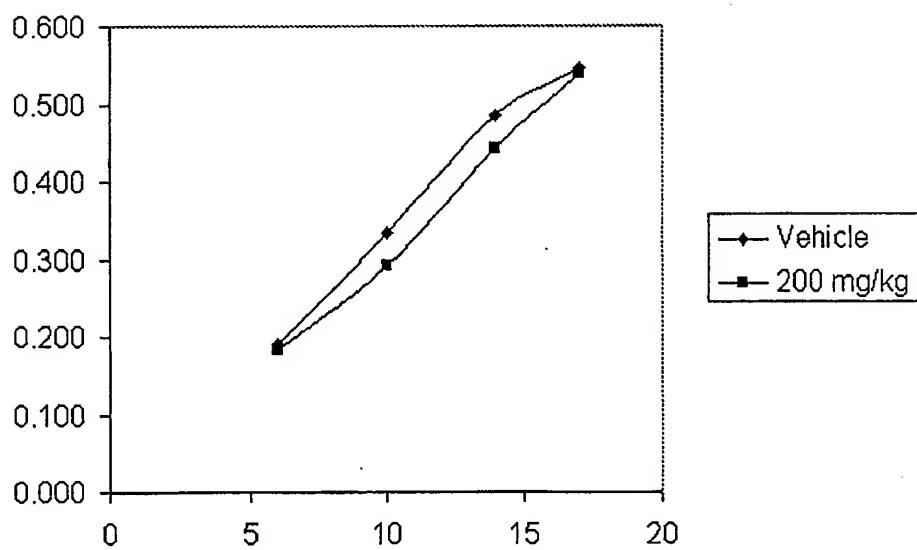
Figure 1**Figure 2**

Figure 3

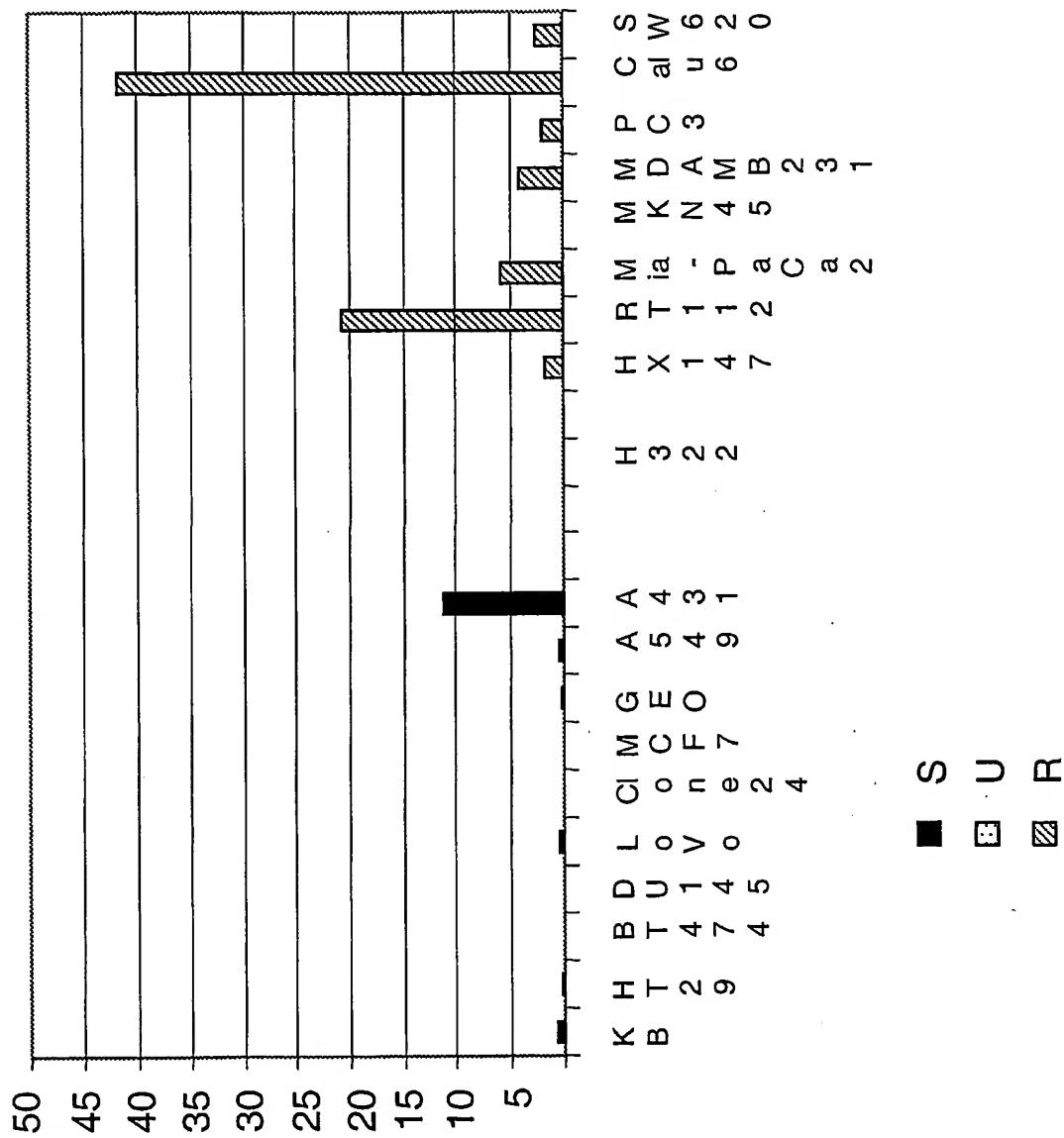


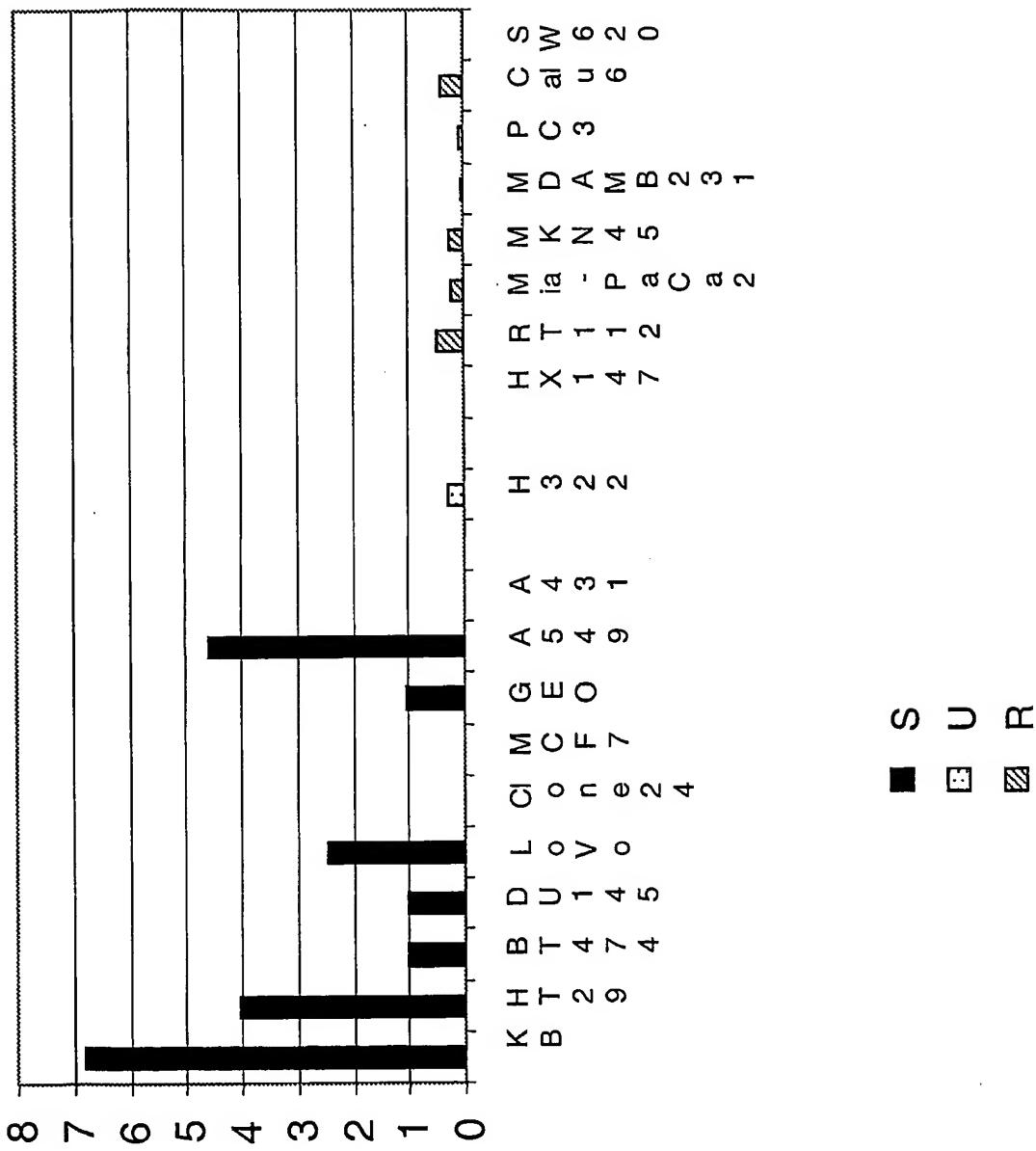
Figure 4

Figure 5

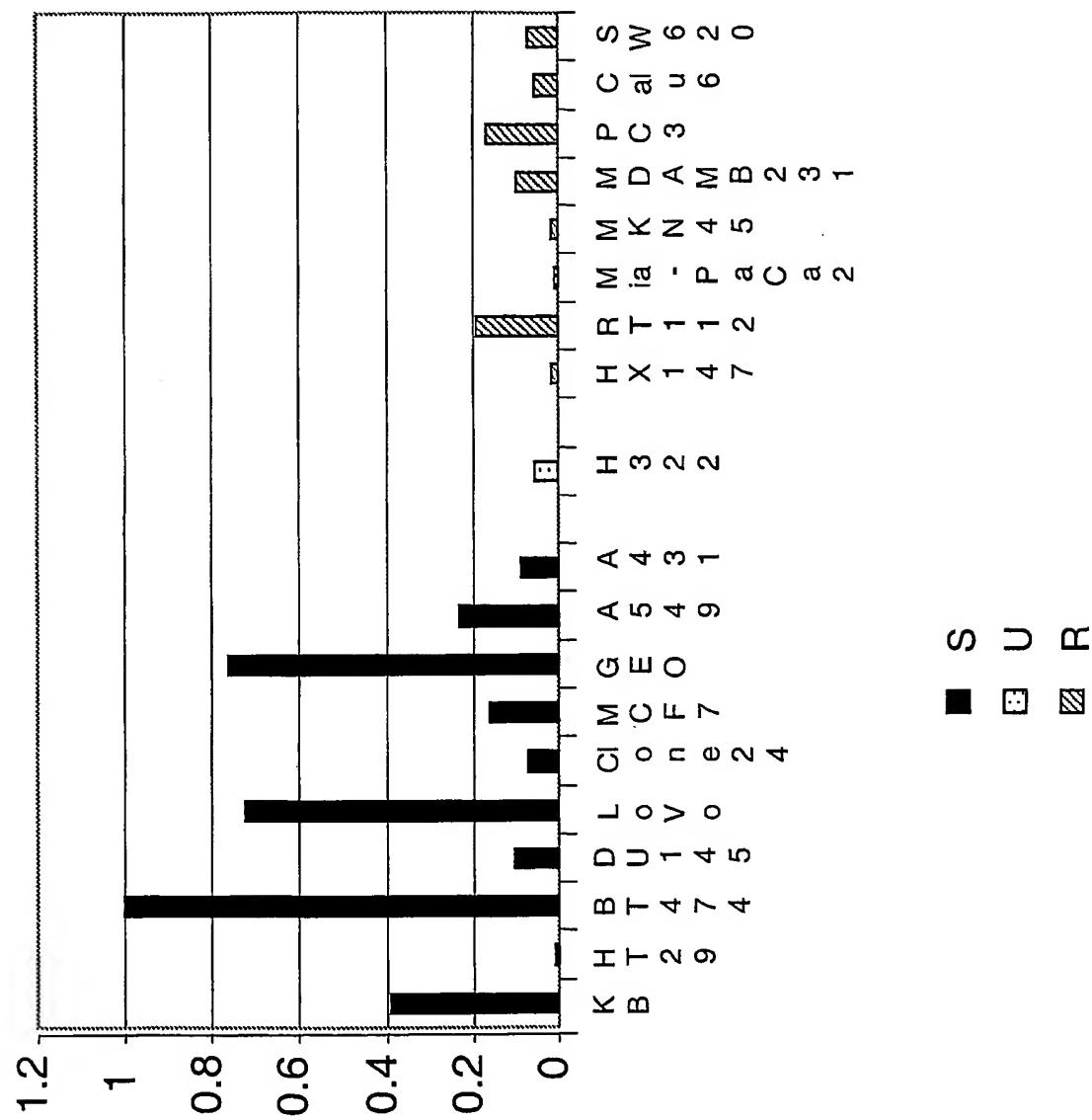
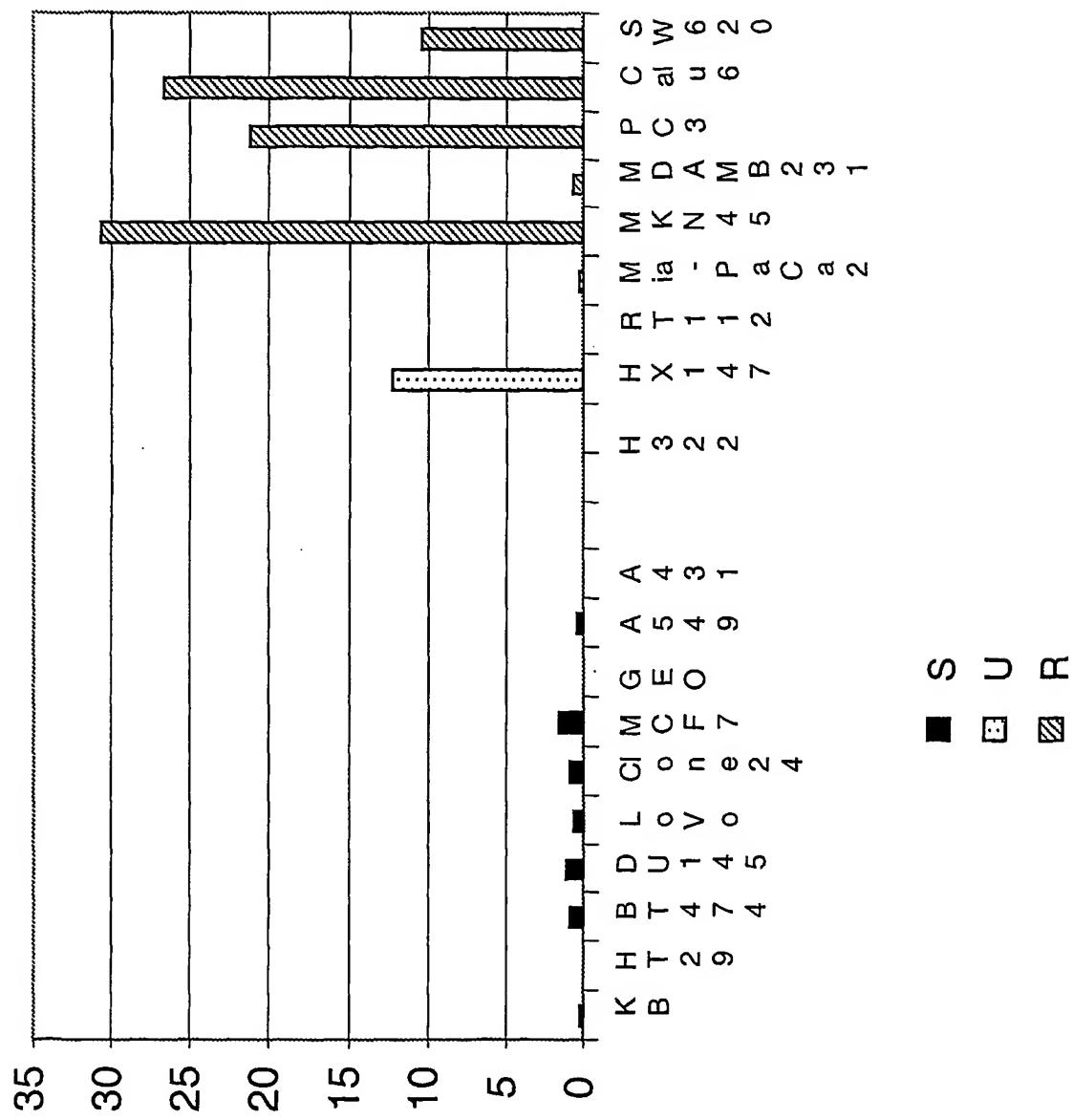


Figure 6

1

<110> AstraZeneca AB

<120> METHOD

<130> CCH 101515

<140> · US 60/590357 and US 60/619027
<141> 2004-07-23

<150> US 60/590357 and US 60/619027
<151> 2004-07-23

<160> 142

<170> PatentIn version 3.2

<210> 1

<211> 425

<212> DNA

<213> Homo sapiens

<400> 1

gtgcagcatt tacagaccct gacgcaatcc ggagctgacc agcacgaggc ttggAACCG 60
accactgtca tacacctcca ggctgctaag gtgcactgct actatgtcac tgtgaagggt 120
tttacagaag ctctggagaa actagaaaat gaaccagcga ttcagcagggt gctcaagcgc 180
ctctgtgacc tccatgccat acatggaatc ttgactaact cgggtgactt tctccatgac 240
gccttcctgt ctggtgccca agtggacatg gcaagaacag cctacctgga cctgctccgc 300
ctgtatccgga aggatgccat cctgttaact gatgctttg acttccaccga tcagtgttta 360
aattcagccc ttggctgtta tgatggaaac gtctacgaac gcctgttcca gtgggctcag 420
aagtcc 425

<210> 2

<211> 507

<212> DNA

<213> Homo sapiens

<400> 2

gagcttaaga tctgggttt tggtaatgtc tctgtttatt ccagaagcat taaggtaacc 60
cattgccaaag tatcattctt gcaaattatt ctttatata actgaccagt gcttaataaa 120
acaaggcaggt acttacaaat aattaactggc agtaggttat aattggtggt taaaaataa 180
cattggaata caggacttgt tgccaaattgg gtaatttca ttagttgttt tgtttggttt 240
gatttgaaac ctggaaatac agtaaaattt gactgtttaa aatgttggcc aaaaaaatca 300
agatttaatt ttttatttg tactgaaaaa ctaatcataa ctgttaattc tcagccatct 360
ttgaagcttggaaagagt ctttggatt ttgtaaacgt tagcagactt tcctgccagt 420
gtcagaaaat cctattttagt aatcctgtcg gtattccttg gtatctgaaa aaaataccaa 480
atagtaccat acatgagtta tttctaa 507

<210> 3

<211> 348

<212> DNA

<213> Homo Sapiens

<400> 3
 agaatagaga ggaggcttga aggaaccagc aatgagaagg ccagggaaaag aaagagctga 60
 aaatggagaa agcccaagag ttagaacagt tggatacagg agaagaaaca gcggctccac 120
 tacagaccca gccccaggtt caatgtcctc cgaagaatga agtctttccc tggtgatggt 180
 cccctgcctt gtctttccag catccactt cccttgtctt cctgggggca tatctcagtc 240
 aggca gggc ttccctgatga tggtcgttgg ggtgggtgtc atgtgatggg tccctccagg 300
 ttactaaagg gtgcattgtcc cctgcttgaa cactgaaggg caggtggt 348

<210> 4
<211> 487
<212> DNA
<213> Homo Sapiens

<400> 4
 aactcatacg tcctgtggtg gcattggag agttcccca ttagtgggc caagatagaa 60
 tctgtaccac tcagtgtcacatccccacc cctacaccac ttccacacag gggcctcatg 120
 gcatggtcag ggtcccaagct gtaggtgaga gcaggcact gtcagctgt ccactgggaa 180
 agtcaagatg tcctaaggcc caggtcaggg catctggagt ctgaaggacc ctatcccta 240
 gaggcatctg gcagcaagaa ggtgaggcat cagggAACGG gaatcaggct gggactgatc 300
 agaggtgaag ggacagagag aggagaggag gaagattgag ctgggggcaa cagccaaagct 360
 cacctgggca ggtctctgcc acctccttgc tctgtgagct gtcagtc tagtattctt 420
 tttttgtgg ctatTTTAA ttgctttggaa tttgttaat gttttctgtc ttctgttaag 480
 tgtgttt 487

<210> 5
<211> 318
<212> DNA
<213> Homo Sapiens

<400> 5
 tgaacggctg tgcagtaggc ccagcgctgc tgtgtctcg t cagaggaata gcttaccac 60
 aacccctcag catactggga atctcttctt gaacaacgaa tgtaaattttt gtcaagtctt 120
 ctatccgtt cattcaatta ttttaagcat ttgaattttt tattgtatat cctaaatata 180
 tttctccctt ggcagtgact agatTTCCAC taatgtgtct taatctatcc ctccagctgg 240
 cagttactgt ttttttaatc ccctgaagtt gtcctgtagg agacagaaaat tttttgtgt 300
 ctgtatccct tggagtaa 318

<210> 6
<211> 135
<212> DNA
<213> Homo Sapiens

<400> 6
 gaggcaaatg gatctcgata tttcagatgg gctttgtatg cactgttgcc aaggaaggct 60
 ttttctgatt ttttgacaaa tgaatttttgcacacttca ttgggtgttt tcggcaacctt 120
 acacacattt aaaaat 135

<210> 7

<211> 402

<212> DNA

<213> Homo Sapiens

<400> 7

caagttttgg tggcacgcag cctggggact ctgcctcggt	ccgctgagcc tggcgcagat	60
cgatttgaat ataacctgco gctttgcagg tgtattccac	gtggagaaaa atggtcgcta	120
cagcatctct cggacggagg ccgctgaccc ctgcaaggct	ttaaatagca ccttgcac	180
aatggcccag atggagaaag ctctgagcat cggatttgag	acctgcagtt tgcattgcag	240
tcaacagtgc aagaagggtgt gggcagaaga aaaagctagt	gatcaacagt ggcaatggag	300
ctgtggagga cagaaagcca agtggactca acggagaggc	cagcaagtct caggaaatgg	360
tgcatttgtt gaacaaggag tcgtcagaaa ctccagacca	gt	402

<210> 8

<211> 417

<212> DNA

<213> Homo Sapiens

<400> 8

attgttaatac ttttgtgtct cctgaagact tcccttaaaa	ttagctctga gtaaaaatc	60
aaaagagaca aaagacatct tcgaatccat atttcaagcc	tggtagaatt ggcttttcta	120
gcagaacctt tccaaaagtt ttatatttag attcataaca	acaccaagaa ttgattttgt	180
agccaacatt cattcaatac tgttatatca gaggagtagg	agagaggaaa catttgactt	240
atctggaaaa gcaaaaatgtt cttttaaaaata agaataaacat	ggtccattca cctttatgtt	300
atagatatgt ctttgtgtaa atcatttgtt ttgagtttc	aaagaatagc ccattgttca	360
ttcttgtgtct gtacaatgac cactgttatt gttactttga	cttttcagag cacaccc	417

<210> 9

<211> 546

<212> DNA

<213> Homo Sapiens

<220>

<221> misc_feature

<222> (104)..(104)

<223> n is a, c, g, or t

<400> 9

ttctatgcat ccacaccaaa atcctgcaga atgtaagtaa	gctctgcttt ataagatggg	60
ttcaccttca tcgcagactg aaagttttag ttttatttt	tttncagaaa gcacgaaaaa	120
ttatttataa tagtctggag aaaaaacaca ctgtaatatt	tcaagtgtat gcagtagaat	180
gtactgtAAC tgagccctt cccacatgtc taggctccaa	tgtctcctgt aggtccacct	240
aactgtgtgt tttcagggac aatgccatcc atgtttgtgc	tgtagacttg ctgctgctga	300
atcccttctg gggactttct catcgggcag ggagcagagg	gcttctcggtt catgcaccc	360
ttgcctgaac acccatgttag ctgctgtgtt gtgtatata	tactcttaag aggagtgtgt	420
gtgtctgtgt ttgtttaaa agtcacttat ttcttacagt	gatttcaatt gcaccatgac	480
ttcttcacta aaaccacaaa gtcctgccta aaactatgga	aaacctaacc tgattagac	540
cttgac		546

```

<210> 10
<211> 546
<212> DNA
<213> Homo Sapiens

<400> 10
ggcaatctgt cacactctca gagtctggga cttgacttgc taccacaac tgctgtgcaa      60
ttctgctgag caggaatatac atgagctgtt caataatgac ggacgcattt gttgagatga     120
agttccagt aaggaagtga cagtgcata tggatattta tggctgtaaa ataggaagag     180
cttagttcc caggctgaac ctgccactgc tggagccatt tcaacaaggc atcctcacaa    240
caaagaagag atgtgatttg gtaccatttc acaccaggc gtgtctggac gaaaacatca    300
atgtgaataa gggccaagtgc cagtgcata ttgattaaat tacttaataa tattattaaa    360
taataatagg tctggcagt attgtttta acctgactca tccagctgtc cttcaaatacg    420
ctccgtctcc ctctacccag aactgatttt taaaaaagaag taattttctt ccctggctg    480
ggaaaaccct aatgaactga aacacacttt tacttaaaaa ttttctgtc tggcgtttt    540
gtaatc                                         546

<210> 11
<211> 496
<212> DNA
<213> Homo Sapiens

<400> 11
gaattcccta gaaatcctac tgggaagtat aggcagatct ctccctcata taacggatgt      60
ttcttggcgc ttggaaatatac agataaagac caatcaactt cataggatgt acagacctgc    120
atatttggtg accttaagtgc tacagaacac tgattccccca tcctatccag agatttagtt    180
tagttgcagc atggaacaat tacaggactt ggtggggaaa cttaaagatg ctgcggaaag    240
cctgaaaaga gcaactcagt tgtaacttgg ggaagttaac gatccgcccgg agtgcagagg    300
aaaaccagaa acgccttgcc ttcaagctgaa ccaccgtttt tgcgagctgg atgtcctttt    360
cagtagaaaa gaattttctt ttgaaattta taccattcat caattttgac actttaaaaaa    420
cgtgtgaaag ggttaagagg gaaagatact gcccaagtat ttgaatcggt tagtagtaac    480
tgtccattta tcctat                                         496

<210> 12
<211> 313
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (190)..(190)
<223> n is a, c, g, or t

<400> 12
tataatactt cagtaaggcc tttaaaaaat ccacagtgtt attattactc ctaacaaaaaa      60
caataattac ttagtatcat ctaatatgtt gttcatattt aaattttttt ttttgagatg     120
ggcttacaa ttggtttttattt caattgcatt ttttcttaact cgtgtctcaa gtgtttttaaa    180

```

5

aatctactgn acttataatg acttatataaa tgtatccctc atttacatt tcttccaaaa	240
gagggaaataa tggcaaacca tataatattg tacattcaact gtcaaaaagc aaacccttgt	300
tttgataact tgt	313
<210> 13	
<211> 395	
<212> DNA	
<213> Homo Sapiens	
<400> 13	
cctctccag ggtgattta tgatcagtgt tggtgccta ggaagacatt ttccgttg	60
ctttgttcc aatgtcaatg tgaacgtcca catgaaacct acacactgtc atgcttcata	120
attccctctc atctcaggta gaagggttag acagggttag ggtagacag acctatgtaa	180
gaattcagaa gacccctgac tcatacatgg tggcagtccc ttataattgg tgcatagcag	240
atggtttcca catttagatc ctggtttcat aacttcctgt acttgaagtc taaaagcaga	300
aaataaagga agcaagttt cttccatgtat tttaattgt gatcgagttt taaattgata	360
ggagggaaaca tgcctaatt cttctgtcct gagaa	395
<210> 14	
<211> 569	
<212> DNA	
<213> Homo Sapiens	
<400> 14	
aggagaggat ttgccactgc ttttctaagg acgagaagcc tggtgaagct attagggttt	60
gttctgaagt ttacagatg gaacctgaca atgtgaatgc cctgaaagat cgagctgagg	120
cctatttgat agagggaaatg tatgtaaatg ctatccatgg ttatgaaact gctcaggaac	180
acaatgaaaa tgatcagcag attcgagaag gtctagagaa agcacaaaga ttattgaaac	240
agtgcagaa acgagattat tataaaatct tgggagtaaa aagaaatgcc aaaaagcaag	300
aaattattaa agcataccga aaattagcac tgcagtggca cccagataac ttccagaatg	360
aagaagaaaa gaaaaaaagct gagaaaaagt tcattgtat agcagctgct aaagaagtcc	420
tctctgatcc agaaatgaga aagaagttt acgacggaga agatcctttg gatcgagaga	480
gccagcaagg aggcggcgcc aacccttcc acagaagctg gaactcatgg caagggttca	540
atcccttcag ctcaaggcgga ccattttaga	569
<210> 15	
<211> 481	
<212> DNA	
<213> Homo Sapiens	
<400> 15	
tgagggccac gggcttgggt agtggaaagg gtgtttggga aattgttaaa tcagttaccc	60
gttagtagagc tatttttgtt acttctaagt tttctagaag tggaggatt gtatgtcatcc	120
tgaaaaatggg tttacttcaa aatccctcag cttgttctt cacgactgtc tataactgaga	180
gtgtcatgtt tccacaaagg gctgacaccc gacgtggat tttcaactcat ccctgagaag	240
ccctttccag taggggtggcc aattcccaac ttccctgcca caagttccc aggctttctc	300
ccctggaaaa ctccagttt agtcccagat acactcatgg gctgcccctgg gcagccagca	360

ttcattgtaa gttccctt taaaaactgg tgtgtgggtg ttcaagttctg tgtctgggg	420
gtatggacag acagtaatct cctgtatct gtgctagctg tgaggcagct ctggaacgtg	480
a	481
<210> 16	
<211> 398	
<212> DNA	
<213> Homo Sapiens	
<400> 16	
ggctcccagc aaggtagga cggggccat gcgggcagaa agttgggact gagcagctgg	60
gagcaggcga ccgagctct tccccatcat ttctcttgg ccaacgacga ggccagccag	120
aatggcaata aggactccga atacataata aaagcaaaca gaacactcca acttagagca	180
ataacggctg ccgcagcagc cagggaaagac cttggtttg tttatgtgtc agtttcactt	240
ttccgataga aatttcttac ctcattttt taagcagtaa ggcttgaagt gatgaaaacc	300
acagatcta gcaaatgtgc ccaaccagct ttactaaagg gggaggaagg gagggcaaag	360
ggatgagaag acaagttcc cagaagtgcc tggttctg	398
<210> 17	
<211> 499	
<212> DNA	
<213> Homo Sapiens	
<400> 17	
gatacgctgg gccccatgca gaaggagctg gccgagcagc tggcctgtc tactggcgag	60
aaggagaagc tgccgggaga gctagagccg gtgcaggcca cgccagaacaa gacagggaaag	120
tatgtgccgc cgagcctgct cgacggggcc agccgcccgc gggagtccat gcagccaaac	180
cgcagagccg acgacaacgc caccatccgt gtcaccaact tgtcagagga cacgcgtgag	240
accgacactgc aggagctttt ccggccttgc ggctccatct cccgcattca cctggctaag	300
gacaagacca ctggccaatc caagggcttt gccttcatca gcttccaccc cgccgaggat	360
gctgcgcgtg ccattgcccgg ggtgtccggc tttggctacg accacctcat cctcaacgtc	420
gagtgggcca agccgtccac caactaagcc agctgccact gtgtactcgg tccgggaccc	480
ttggcgacag aagacagcc	499
<210> 18	
<211> 261	
<212> DNA	
<213> Homo Sapiens	
<220>	
<221> misc_feature	
<222> (41)..(42)	
<223> n is a, c, g, or t	
<220>	
<221> misc_feature	
<222> (196)..(196)	
<223> n is a, c, g, or t	
<400> 18	
atgtgtcggg gagagagccc gcagggaaagg gtaaagccca nnngggcagg gcccctccag	60

atgcctgagg agggggcagg tccccctccc ttccttcctc ttccctcccc atctaaaggg	120
gtttggggag agacacaggc aggcgagggg gctggtcccc agtctgttgg ggtggtgctc	180
aggtaaagg gctatngca acaggggacc agaccaggga tgagtgggga gggcacaagg	240
accatttgcc agaatccacc g	261

<210> 19
<211> 526
<212> DNA
<213> Homo Sapiens

ctgtgctcc agatgcatt ctgataggag gggcgccag ggctggccct tgtgacaatc	60
tgccttcac cacatggcct tgcctcggtg gccctgactg tcagggaggg ccagggaggc	120
agagcgggag ggagtctcag gaggaggctt gccctgaggg gctggggagg gggtacctca	180
tgaggaccag ggtggagctt gagaagagga ggaggtgggg gcttggaggt gcttggtagc	240
tgaggggacg ggcaagttag aggggaggg gggaaatgcctt gggaggatcc tgagctgt	300
ttgcagtcta acccactaat cagttcttag attcagggga agggcaggca ccaacaactc	360
agaatggggg ctttcgggaa gggcgccatg tccccccagc tctaaggcagc caggagggac	420
ctgcatctaa gcatctgggt tgccatggca atggcatgcc cccagctac tgtatgcccc	480
cgaccccccgc agaggcagaa tgaacccata gggagctgat cgtaat	526

<210> 20
<211> 516
<212> DNA
<213> Homo Sapiens

gggaccaccc statagtgtat ctggcgatc tcatgtcg gcacggctgg cgcacaggcg	60
ccatcatccc cgagctggag cgtgagatcc gcatacatcaa cacggagcag tacatgcact	120
cgtacgtg gcagcaggcg ctcacggggc tgctggagcg catgcagacc tatcaggacg	180
cggagtcgag gcaggtgctg gctgcctgga taaaagagcg gcaggagctg aggtgcata	240
ccaaggccct gttcaatgcg cagttcgca gcataatccg caccttccac aacccaccc	300
acttctcaag ggcctcgat cgatctctg acctctacat ggctccctc agctgcctgc	360
tcaactaccg cgtggacttc accttctacc cacccgtac gccgctgcag cacgaggcac	420
ccctctggat ggaccagctc tgcaccggct gcatgaagac ccccttcctt ggtgacatgg	480
cccacatccg ctgagggcac ctttattgtc tggcac	516

<210> 21
<211> 482
<212> DNA
<213> Homo Sapiens

tattcaaacg gagtcctccc attccaagaa actggaaacc cctagtttat gttaaaaggc	60
cagtctaaat tctttactt acatcttac agaaaactat atttctctc ttccatacc	120
agaaatctaa tcagaaaact gactttctc atgttcaact ggacctaggg gaatatgaca	180

8

gaaaaggcatc ccataggctt taatatactt tttaaaatat ataaaaactga aaattaatag	240
ccatttaccc tgaaagagtt ctgcgtggac tttgtcaactt gcatagtaat agcatgtgcc	300
tcattgttca gaagattagc tttaggtctt atttcaaat acgaaatggt agcataagct	360
gtaaaaactgt agtcttctct gcagaaaaata aaggccaaca ataagaaaago ttttgaagga	420
atcacggaaa acaaatttat aaaagaaata actatatgcg cagtaattct taacacattg	480
ac	482

<210> 22

<211> 459

<212> DNA

<213> Homo Sapiens

<400> 22

gcaagtgcgc tgatttctac cacacctgct actgcctgag cggcctgtcc atagcccagc	60
acttcggcag cggagccatg ttgcattatg tggccttggg tgtgcccggaa aacgctctgc	120
agcccaactca cccagtgtac aacattggac cagacaaggt gatccaggcc actacatact	180
ttctacagaa gccagtcaca ggaaaaagg agcttaagga tgagacatcg gcagagcctg	240
caaccgacta gaggacctgg gtccggcag ctcttgcac acccatctcc ccagtcagac	300
aaggttata cgtttcaata catactgcac tctgtctac acaaggccta gcctcagtgg	360
agctgtggtt ctcttggat tttttgtca aacaaaacca atggctctgg gtttggagaa	420
cacagtggct ggaaaaaaa ttcttccac acctgtcaa	459

<210> 23

<211> 549

<212> DNA

<213> Homo Sapiens

<400> 23

tgtatgcacc tagcagggttc ccactaggat gcagagatga cctctcgctg	60
cctcacaaggc agtgcacacct cgggtccctt ccgttgctat ggtggaaatt cctggatgga	120
atggatcaca tgagggttcc ttgttgcattt tggagggtgt gggggatatt ttgttttgtt	180
ttttctgcag gttccatgaa aacagccctt ttccaaagccc attgtttctg tcatggtttc	240
catctgtcct gagcaagtca ttcccttgcattt atttgcatt tcgaacatct cggccattca	300
aagcccccat gttctctgca ctgtttggcc agcataaccc ctgcgcattca	360
agtttaacc tgacggcatg gaatgtataa atgagggtgg gtccttctgc agataactcta	420
atcaactacat tgctttttct ataaaaactac ccataaggct ttaaccttta aagaaaaatg	480
aaaaagggtta gtgtttgggg gcccgggggg gactgaccgc ttccataagcc agtacgtctg	540
agctgagta	549

<210> 24

<211> 372

<212> DNA

<213> Homo Sapiens

<400> 24

aagcaattttt cttgatgcct ctgcaagata ctgtgaggag aattgcacagc aaaagttcac	60
cacctactct tatattactgc ccattgatttgc acttttcttc atatatttgc aagagaaaatt	120

tcacagcaaa aattcatgtt ttgtcagtt tctcatgttg agatctgtta tgtcactgat	180
gaatttaccc tcaagttcc tteectctgta ccactctgct tccttggaca atatcagtaa	240
tagctttgta agtcatgtgg acgtaattgc ctacagtaat gaaaaattaa tgtactttaa	300
tttttcattt tcttttagga tathtagacc acccttggtc cacgcaaacc agagtgtgtc	360
agtgtttgtg tg	372

<210> 25
<211> 475
<212> DNA
<213> Homo Sapiens

cagggatcg aggacgaccc gagtcccaag agtggggttt tgcttttaa aaggagagag	60
gaggggtgat ggcaggggag tggaggggtgg cccggcaggc cctgccggcg cagggagccc	120
tctgcccttc acactctcct ccaaaagagc ctccatctgt aaggaagcag gtctccgcga	180
ggggtttctt tccatgtgtt ttccctctgt tgttaaaaga acttttttaa aaaaacagac	240
ctcgttttag atttagca ttgactttta cacacattca cacaagaaaa aaatcccttc	300
aaaattctta aatcttctgt tccatgtttt tccaaggaa gagggcaaaa agtggctgg	360
gctctgttgg tgtgcgtgtt ccgtggcgga gagaagaaaa tggaaagac atctcactgg	420
tgctttctc ttttgtttta gtgcggcccg ccccatccc tataatatct gtaac	475

<210> 26
<211> 516
<212> DNA
<213> Homo Sapiens

gaagcaattt ctcatgttgg ccaaacatgg tgcacccgagt gattccatc tctggtaaag	60
ttacactttt atttccatgtt tggtgtacaa tcaaaacaca ctactacatc ttaagtccca	120
gtataacctca tttttcatac tgaaaaaaaaa agcttgcggc caatggaaca gtaagaacat	180
cataaaattt ttatatatat agtttatattt tggggagat aaattttata ggactgttct	240
ttgctgttgg tggcgcggc taaataagac tggacattta actttctac catttctgca	300
agtttaggtat gtttgcagg agaaaaagtat caagacgttt aactgcagtt gactttctcc	360
ctgttccttt gagtgcgttc taactttattt ctttgttctt tatgtagaat tgctgtctat	420
gattgtactt tgaatcgctt gacttgtga aaatatttctt ctgtgtatt atcactgtct	480
gttctgcaca ataaacataa cagcctctgt gatccc	516

<210> 27
<211> 566
<212> DNA
<213> Homo Sapiens

gcgtttccaa cctcggagaa ttccaggcac tccccctccc cctccgctga catacttgta	60
taagcggtca tcgttgcgtc atggggcagg cgtggggagc ttccctgtcgcc tttggctgg	120
tgtggccctg gaggaaaggc cttggggcgtg cactcgccctg ggcagtgcccc aggagatgg	180

10

cctgagttac	ttcacccccc	cgtgctgctg	gttaatgtcc	cgcgtctctg	caccccccgg	240
tgggagcggg	gactgatcta	cttcacatt	ctcaagttt	tctcatctgc	attagaggtc	300
cccaagttagt	tcccagggttc	cagcgtgcc	ctccctcaga	cacacggaca	caatcagccg	360
agaagttcct	ggtctgaatc	acgagaatgt	ggaggggtgg	gggggtgtcag	tggaaaggca	420
taaggctgag	ctgagaccag	ttgctggtga	aactgggcca	atctggggag	ggaaacatcc	480
ttgccaggga	gtttctgagg	gtctgctttg	tttaccttgc	gtgcgggtgg	ttctttttaa	540
ctccgtctac	ctggcgcccc	ttttaga				566

<210> 28
<211> 327
<212> DNA
<213> Homo Sapiens

<220>						
<221> misc_feature						
<222> (199)..(199)						
<223> n is a, c, g, or t						
<400> 28						
ccacctgtga	ccccgtggtg	gaggagcatt	tccgcaggag	cctgggcaag	aattacaagg	60
agcccgagcc	ggcacccaaac	tccgtgtcca	tcacgggctc	cgtggacgac	cactttgc	120
aagctctggg	tgacacgtgg	ctccagatca	aagcggccaa	ggacggagca	tccagcagcc	180
ctgagtcgc	ctctcgcaang	ggccagcccg	ccagccctc	tgcccacatg	gtcagccaca	240
gtcaactcccc	ctctgtggtc	tcctgaaggg	agcgcctct	ccaacaacac	gtggatctgc	300
atggtttgc	tgagctttga	acagtca				327

<210> 29
<211> 347
<212> DNA
<213> Homo Sapiens

<220>						
<221> misc_feature						
<222> (156)..(156)						
<223> n is a, c, g, or t						
<400> 29						
attagtctcc	aaggcattca	gtgatgtctt	cagcatca	ataggactgt	ctagtgtcac	60
tttttacttc	cttctgggtg	gaggcttcc	gactccaaat	catgaaggca	agttaatctt	120
tccagttgt	gactttgcc	ccatagttgg	ggtaanact	tcctagattg	agaaaaagca	180
gctacagtca	atccgtctc	gtttgcctca	tttgggtgate	agtcaagtac	acataaggtc	240
cttgttattct	aaatttcatg	cacttctccc	agatgtata	gggtttctc	tcactgttgc	300
caatggatgt	catccagaca	gtgggctcat	atcttacggt	tttgtgc		347

<210> 30
<211> 210
<212> DNA
<213> Homo Sapiens

<400> 30						
agtgtatcag	agccttccag	agtgtggtat	gctttcaact	gtgtgatgat	ccttagtggc	60

11

acatgaatga acgtccagat gtttgcag tagcccaccc ttatctgcag gatacgttcc	120
aagaccccca gtgaatgcct gaaactgcag atagtaactga atccttatata tactgtgttt	180
tttatgatac atacatgcct atgatgaagt	210

<210> 31
<211> 511
<212> DNA
<213> Homo Sapiens

<400> 31	
aagagaatgt tcctactcac acttcagctg ggtcacatcc atccctccat tcatccttcc	60
atccatcttt ccatccatta cctccatcca tccttccaac atatatttat tgagtaccta	120
ctgtgtgcca ggggctggtg ggacagtggt gacatgtct ctgcctcat agagttgatt	180
gtctagttagtgaagacaaggc atttttaaaa aataaattta aacttacaaa ctttgtttgt	240
cacaagtgggt gtttattgca ataaccgctt ggtttgcAAC ctctttgctc aacagaacat	300
atgttgcaag accctccat gggggcactt gagtttggc aaggctgaca gagctctggg	360
tttgtcacat ttctttgcat tccagctgtc actctgtgcc tttctacaac tgattgcaac	420
agactgttga gttatgataa caccagtggg aatttgttgg agaaccagag gcacttccac	480
cttggctggg aagactatgg tgctgccttg c	511

<210> 32
<211> 505
<212> DNA
<213> Homo Sapiens

<400> 32	
aaggcattcc acaggatcat catttaaaaaa aaaagaattc tggcctgtt ttctaaaaaaaa	60
aaaaaaaaactgt ttagaaattt cttatattgg atctatTTT tagtcagagt ttcaGTTTC	120
ttcagctgcc agtgtgttac tcataTTT cttaaaaatc tggaaatcaga gatTTTTGTT	180
tgttcacata tgattctttt agacactttt atattgaaa aaattttttt ctTTTTGG	240
ggaaaaattt ttggTTATTC tgccataaca gattatgtat taacttggtag attcagtgg	300
tcaatacccg ttttagttgtc tgctaatatt tccagaagga ttcttgcatt tggtgaaaga	360
cgggtgggaa tggggggatt tttttgtct tgggtaccc ttgtttgaa actagaaatc	420
tgtcctgtgg catgcaaaag aaagcaaattt atttttaaaaa gaaaaaaacc aaagtacttt	480
tgggtgtcatt attccatottt ctcca	505

<210> 33
<211> 307
<212> DNA
<213> Homo Sapiens

<400> 33	
ccagccactg cagatagaga catatggacc acatgttccct gagcttggaga tgcttaggaag	60
acttgggtat ttaaaccatg tcagagctgc ctcaccacag gaccttgctg gaggctatac	120
ttcttctttt gcttgcaca gagcactaca ggatgcattc agtggggctt tctggcagcc	180
cagttaacca ttataaagat ttggacccctt gagctgaacc agggagctag caaaaagtaaa	240

12

gcagacttat	aaaattatag	ctatgtcag	ctgcacaaca	cagtcccttc	actagcagct	300
gtgttaa						307
<210> 34						
<211> 519						
<212> DNA						
<213> Homo Sapiens						
<220>						
<221>	misc_feature					
<222>	(130)..(130)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(144)..(144)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(167)..(167)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(169)..(169)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(268)..(268)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(349)..(349)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(358)..(358)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(478)..(478)					
<223>	n is a, c, g, or t					
<400>	34					
caccgcgcag	agtcagggg	gtgggtcgcc	cggcccttct	gccccgcaca	gcccaagccca	60
ggaacgcggg	cgggtcgccgac	ttagcgggccc	gggtgcaggc	gccccggctgg	gcctctgcgc	120
ccggcccgan	ctccgtctat	aaanagagca	gccaggttgca	gggctcnant	ctgctttcca	180
actgcctgac	tgttgttcg	tctcactggt	gtgagctcca	gcataccctt	tgctcgaaat	240
ggaccccaac	tgctcttgcg	ccactggntg	gctccctgcac	gtggccggc	tcctgcaagt	300
gcaaagatgt	caaatacgacc	tcctgcaaga	agagctgtct	ttccctgtnc	cccggtggnc	360
gtgccaagtg	tgcccagggc	tgcgtctgca	aaggggcatc	ggagaagtgc	agctgctgt	420
cctgatgtgg	gaacagctct	tctccagat	gtaaatagaa	caacctgcac	aacctggnat	480
ttttttaaaa	ataacaacact	gagccatgg	ctgcatttc			519

<210> 35

<211> 460

<212> DNA

<213> Homo Sapiens

<400> 35

gcagcactct	taacttacga	tctttgaca	tacggttct	ggctgagagg	cctggccgc	60
taagggtaaa	aggggtgtgg	caaaggagcc	tactccaaga	atggaggctg	taggaataata	120
acctccccacc	ctgcaaagggg	aatctcttc	ctgctccatc	tcataggcta	agttagtga	180
atcccgatag	tacttaggtcc	ccttccctcc	gcattccgtc	agctggaaaa	ggccctgtggc	240
ccagaggctt	ctccaaagggg	agggtgacat	gtggctttt	gtgcccaga	tcaccagccc	300
tgcccacct	cactgcagta	gtgcaccatc	tcactgcagt	agcacgcct	cctggcccg	360
ctggcctgtg	gctaattggag	gtgacggcac	tccatgtgc	tgactcccc	catccctgcc	420
acgtgtggc	cctgcctggc	tagtccctgc	ctgaataaaag			460

<210> 36

<211> 540

<212> DNA

<213> Homo Sapiens

<400> 36

gctacagatt	cacactttct	ggcctaaacc	ctaattggat	gaggcttttc	accccaggcc	60
atgctgggtgg	tgatTTTTA	gcccctaaat	aaaacactgg	actatTTTc	tttacttca	120
ttgattgcaa	ctacaaaggt	ggactcaaag	caaagcacaa	tcatgccagc	caacattcca	180
gaattctgct	gagaactcca	agtctgtgag	gggagagggtt	ttacaagcca	gacaggctg	240
ggggactgca	gtccccaaagg	agaccctgcc	acatgtggc	cctttgagtg	agaatgctgc	300
atctttctac	atatcttcat	gagaatactg	agaattggat	tttcctttt	aaaatgcact	360
ttgctttttt	tgtatgtttt	gttatgtga	gatgtttcta	aagaaaagat	tttatgtaat	420
tataagatga	agcgttagtga	attgtacagc	tgttgtaata	atgacctatt	tctatataaa	480
ataaaaattgt	atggctttagt	tgtaaattat	tttgtatctg	agataccagt	tcctttccc	540

<210> 37

<211> 367

<212> DNA

<213> Homo Sapiens

<400> 37

aaaggggatg	gacgtctcat	tctcaggat	cctgttttc	attgaggatg	tagcccatcg	60
gatgctggcc	acaggcgagt	gtactcctga	ggatctgtgt	tttccctgc	aggaaactgt	120
gtttgcaatg	ctggtagaga	tcacagagcg	agccatggca	cattgtggct	cccaggaggg	180
cctcattgtg	ggaggagtgg	ggtgtatgt	gaggctacag	gagatgtatgg	caacaatgtg	240
ccaggaacgt	ggagcccgcc	ttttgctac	agatgagaga	ttctgtattt	acaatggagc	300
gatgatagcc	caggctggct	gggagatgtt	tcgggatgg	cacaggaccc	cactcagtga	360
ttctggg						367

<210> 38

<211> 532

<212> DNA

<213> Homo Sapiens

<400> 38
cagaaaagtct cagcccagga tggggcttct tcaacaggc ccctgcctc ctgaagccctc 60
agtcttcac cttgccagg gccgtttctc ttccgtgaag gccactgccc aggtccccag 120
tgcgcccccc agtggccata gcctggtaa agttccccag tgcccttcctg tgcatagacc 180
ttcttcctcc acccccctct gcctgggtt ccccgccat ccagcggggc tgccagagaa 240
ccccagacct gcccttacag tagtgtacg cccctccct cttccggctg gtgtagaata 300
gccagtagtg tagtgccgtg tgctttacg tgatggccgg tggcagccg gcccgggct 360
ccgcgcagcc gtctgtcctt gatctgcgg cggccggcccg tttgtgttt tgtgctgtgt 420
ccacgcgcta aggccacccc ctccccgtt ctgacttctc ctataagcgc ttcttcgc 480
atagtacgt agctccacc ccacccctt cctgtgtctc acgcaagttt ta 532

<210> 39
<211> 551
<212> DNA
<213> Homo Sapiens

<400> 39
ggatggggct tcttcaacag ggccctgtcc ctctgtttt ctcaggccctt cacccgttcc 60
gggtgggtt ctcttcgtt aaggccactg cccagggtccc cagtgcggcc cctagtggcc 120
atagcctggt taaaagttccc cagtgccctt ttgtgtcatag accttcttctt cccacccctt 180
tctggccctt ggtccccggc catccagccgg ggctgtccaga gaaccccaaga cctggccctt 240
cagtagtgta ggcggccctt ccttttccgg ctgggtgtt atagccagta gtgttagtgcc 300
gtgtgtttt acgtgtatggc ggggtggcag cggccggccgg gtcggccgca gcccgtctgtc 360
cttgcgcgcgc ccgtgtttgtt ttttgtgtt tgccacgcg ctaaggcgac 420
ccccccccc gtactgactt ctccatataag cgcttcttcc cgcatagtca cgtagctccc 480
acccacccctt cttctgtgtt ctcacgcaag ttttataactt taatattttt atggctttt 540
ttcttcgaca a 551

<210> 40
<211> 538
<212> DNA
<213> Homo Sapiens

<400> 40
gccagcttttggctgagcta acaggaccaa tggatcaaac tggcatttca gtccaaaggaa 60
gctcgaagca ggtttaggac caggtccctt tgagaggtaa gaggggcctc tgggggtgtt 120
gggtacttcca gaggtgtccac tgggtggagg gtcagccgg ccccaacttca tccttgcgtt 180
tagaccccttctt tctcccaccc cttctgtccc ctgggtcccc gcccattccag cggggctgtcc 240
agagaacccc agacctgtccc ttacagtagt gtggccccc cttccctttt cgggtgggtt 300
agaatagcca gtgtgttagt ggggtgtgtt tttacgtat ggggggtggg cagccggccgg 360
cgggctccgc gcagccgtct gtccttgcgtt tgcccgccgc gggccgtgtt gtgtttgtt 420
ctgtgtccac ggcgttaaggc gacccctcc cccgtactga cttcttcctat aagcgcttct 480
cttcgcatacg tcacgttagt cccacccac cttcttcctg tgcgtcacgc aagttttta 538

<210> 41
<211> 403
<212> DNA
<213> Homo Sapiens

<400> 41
tgcacgccc tggcacgtgc actgctttac ctgtgctgcc tgcaagacgc 60
ccatccggaa caggcccttc tacatggagg agggcgtgcc ctattgcgag cgagactatg 120
agaagatgtt tggcacgaaa tgccatggct gtgacttcaa gatcgacgct ggggaccgct 180
tcctggaggc cctgggcttc agctggcatg acaccgtt cgtctgtgcg atatgtcaga 240
tcaacctgga aggaaagacc ttctactcca agaaggacag gcctctctgc aagagccatg 300
ccttctctca tgtgtgagcc ccttctgccc acagctgccc cggtgcccc tagcctgagg 360
ggcctggagt cgtggccctg catttctggg tagggctggc aat 403

<210> 42
<211> 437
<212> DNA
<213> Homo Sapiens

<400> 42
tggatccaaa cctttattat gccatttat gatgccagat gaagaaactc cattagcagt 60
gcaggccctgt ggactttctc ctcgagacat taccactatt aaacttctca atgaaaactag 120
agacatgtt gaaagcccag attttagtac agtttgaat acctgtttaa accgaggttt 180
tagtagactt ctagacaata tggctgagtt ctccgtaccc actgaacagg acctgcaaca 240
tggtaactct atgaatagtc ttccagtgt cagctgcct ttagctaaga taattccaat 300
agtaaacgga cagatccatt cagtttgcag taaaacacct agtcattttt ttcaggatct 360
gttgacaatg gagcaagtga aagacttgc tgtaatgtg tatgaagctt ttagtacccc 420
tcagcaactg gagaat 437

<210> 43
<211> 520
<212> DNA
<213> Homo Sapiens

<400> 43
agccatttga agacgcctcg tttgcgtgc ggacggggga gatgagcggg cccgtgttca 60
cggattccgg catccacatc atccctcgca ctgagtgagg gtggggagcc caggcctggc 120
ctcgccccag ggcagggcgg ctaggcccc cagcccccc ttccccgcca gccagtggcc 180
gaacccccc ctcctgcca ccgtcacaca gtatttattt ttccccacaat ggctgggagg 240
ggcccttcc agattggggg ccctgggtc cccactccct gtccatcccc agttggggct 300
gctgaccgcca gattccct taaggaattt acttcagcag gggtgggagg ctccccagacc 360
caggcagtg tgggtggagg ggtgttccaa agagaaggcc tggtcagcag agccgcccc 420
tgtccccca ggtgctggag gcagactcga gggccgaatt gtttctagtt aggccacgct 480
cctctgttca gtcgcaaagg tgaacactca tgcggcagcc 520

<210> 44
<211> 530

<212> DNA

<213> Homo Sapiens

<220>

<221> misc_feature

<222> (68)..(68)

<223> n is a, c, g, or t

<400> 44

gattaaacga ctgtgtcttt gtcacctctg cttaacttta ggagtatcca ttccctgtat	60
tgttagacntt tggatatt ctccctggaa gaatatcatt cttttcttga agggttggtt	120
tactagaata tcacaaatca atcatgaagg cagttactat ttggagtcta aaggtttct	180
aaaaattaac ctcacatccc ttctgttagg gtcttcaga atatctttta taaacagaag	240
catttgaatg cattgtttt gctacatgat ttgtgtgtt gaaggacata ccacgtttaa	300
atcattaatt gaaaaacatc atataagccc caacttggtt tggaggaaga gacggagggt	360
gaggtttttc cttctgtata agcacctact gacaaaatgt agaggccatt caaccgtcaa	420
acaccatttg gttatatcg agaggagacg gatgtgtaaa ttactgcatt gcttttttt	480
tcagtttgc taacctctaa tctccgtttt catgatacgc ttgttagaa	530

<210> 45

<211> 485

<212> DNA

<213> Homo Sapiens

<400> 45

tgaatgtacg cttgtccatg ctgacccatg tgagtataac atgctgtggc atgctggaaa	60
ggctctgggtt atcgatgtca gtcagtcagt agaacctacc caccctcagc gcctggagtt	120
cttggccgg gactgcagga atgtctcgca gttttccag aaaggaggag tcaaggaagc	180
ccttagtgaa cgagaactct tcaatgtgtt ttcaggctta aacatcacag cagataatga	240
agctgatttt ttagctgaga tagaagcttt ggagaaaatg aatgaagatc acgttcagaa	300
gaatggagg aaagctgctt cattttgaa agatgtggc gacccaccac tactatatga	360
tgaatagcac taataccccac tgcttcagtg ttaacacacgc agtgattgtc agctgcaat	420
agcaaatgaa gttatgggtt acttgaaata ccaaaacctg aggagtggc aatggtgctt	480
ctgtg	485

<210> 46

<211> 351

<212> DNA

<213> Homo Sapiens

<400> 46

ttccggcacat tggccgtgtt ggtcttgaac tcctggctc aagcaatccg cctacccat	60
cctcccaaag tgctaggatt acaggcataa gccactgagc ccagccctag ttctgttatct	120
tttatgtaaa ttataaacat ctgcaacatt atgtatcata tgcagatact tattgcattt	180
cttttattag tggtaaaatg gttctatgca ttatggctt cttgaatttc ctcattatg	240
aattgtcatt cacacaccta cttttctgtc tcgttttac atatgtctt gcctattaaa	300
gatattatcc ctctgtttta tattttctct cattcttgc ttgcctttta a	351

<210> 47
<211> 521
<212> DNA
<213> Homo Sapiens

<400> 47
ccggaggcaa agagaccggg ccgcggaggc caaggaaagg gagaacaccg aaaacaataa 60
ctcctcctcc aacaagcaga accaactctc tcctctggaa gggggcaagc cgctcatgtc 120
cagctcagaa gaggattct cacctcccc aagtccagac cagaactcg 240
gcagggcaat atgggccacg ccaggagctc aaactattct ctcccggct taacagcctc 180
gcagccccagt cacggcctgc agacccacca gcatcagctc caagactctc tgctcggccc 300
cctcacctcc agtctggtgg acttggggtc ctaagtgggg agggactggg gcctcgaagg 360
gattcctgga gcagcaacca ctgcagcgc tagggacact tgtaaataga aatcaggaac 420
atttttgcag cttgtttctg gagttgttg cgcataaagg aatggtgac tttcacaaat 480
atcttttaa aatcaaaaac caacagcgat ctcaagctta a 521

<210> 48
<211> 498
<212> DNA
<213> Homo Sapiens

<400> 48
ggctgagcac cagttagttc ttgcctcta ctctgaccct agacaacctg gggagggacc 60
ctgtgcccgc aaaccagaca cataggacaa agtttatcta taacctggaa gaccatgagt 120
ggtgtgaaaa catggagtcc gtttatagt gactaaagga gggctgaact ctgtattagt 180
aatccaaggg tcattttttt cttaaaaaaaaa gaaaaaaaaagg ttccaaaaaaaaa aaccaaaact 240
cagtacacac acacaggcac agatgcacac acacgcagac agacacacccg actttgtct 300
ttttctcagc atcagagccca gacaggattc agaataagga gagaatgaca tcgtcggca 360
gggtcctgga ggccactcgc gcggctggc cacagagtct actttgaagg cacctcatgg 420
ttttcaggat gctgacagct gcaagcaaca ggcactgcca aattcaggga acagtggtgg 480
ccagcttggaa ggatggac 498

<210> 49
<211> 331
<212> DNA
<213> Homo Sapiens

<400> 49
gagacgtggtaagtgcgggt cagtttcaa ctgacctctg gacgcagaac ttcaagccatg 60
aaggtaacag gcatctttct tctcagtgc ttggccctgt tgagtctatc tggtaacact 120
ggagctgact ccctggaaag agaggccaaa tttacaatg aacttaatgg atgcaccaag 180
atatatgacc ctgtctgtgg gactgtatgg aatacttatac ccaatgaatg cgtgttatgt 240
tttgaaggtc gggaaacgcca gacttctatc ctcatcaaa aatctggcc ttgtcgagaa 300
ccaaggttt gaaatccat caggtcacccg c 331

<210> 50
<211> 548

<212> DNA

<213> Homo Sapiens

<400> 50

agccatcca ttttagagct tctcaagagg aagacagccc agactttc agttcttgg	60
attctgagat gtgaaagac taccgagat tgccaggat aggctatctt tgtccaaagg	120
attnaaagcc tgtctgttgt gacgatggcc aaacctacaa caatccttgc atgctctgtc	180
atgaaaacct gatacgccaa acaaatacac acatccgcag tacagggaaat tgtgaggaga	240
gcagcacccc aggaaccacc gcagccagca tgccccgtc tgacgaatga caggaagatt	300
gttggaaagcc atgagggaaa aaataaaccc cagttctgaa tcacccatctt tcaccatctg	360
tatatacaaa gaattcttcg gagcttgctt tatttgctat agaaaaacaat acagagctt	420
tggggatgga atcactgatt ttcaagtctt tccattttttt tccctcttgc atctgtgatc	480
tgagggtata aagacatttc caccaagttt gagccctcaa aatgtcctga ttacaatgt	540
gtctgtcc	548

<210> 51

<211> 526

<212> DNA

<213> Homo Sapiens

<400> 51

gtccacattc ctgcaagcat tgattgagac atttgacacaa tctaaaatgt aagcaaagta	60
gtcattaaaa atacaccctc tactgggct ttatactgca tacaatatttta ctcatgagcc	120
ttcccttgag gaaggatgtg gatctccaaa taaagatttta gtgtttatgt tgagctctgc	180
atcttaacaa gatgatctga acacctctcc tttgtatcaa taaatagccc tggtattctg	240
aagttagagg accaagtata gtaaaatgct gacatctaaa actaaataaa tagaaaacac	300
caggccagaa ctatagtcat actcacacaa agggagaaat ttaaactcga accaagcaaa	360
aggcttcacg gaaatagcat ggaaaaacaa tgcttccagt gcccacttcc taaggaggaa	420
caaccccgta tgatctcaga attggcacca cgtgagcttg ctaagtgata atatctgttt	480
ctactacgga tttaggcaac aggacctgta cattgtcaca ttgcatt	526

<210> 52

<211> 476

<212> DNA

<213> Homo Sapiens

<400> 52

tgggggactt atttgggg gatcttaaat aagatttctt ttgatctacc ggaatataca	60
tgtacagagt acattggatc atgtggaaa gaaggcaagt gaaaagggtca gagatgaagt	120
agcgaagtta tggaaatatcg tggaaaggat actagttgtg aaatggaaag agacaaggta	180
tagtacccca aaagcaaaac aacgaggaga tgcaagagat gccccaaaag gacaaagcaa	240
caattttctg ttgccacccctt tataccggaa gactctgtt tagaagaaaa gaaggctttg	300
gtgcacctta tgtgggagga ggagggcag ggcacgttgc tgctgagcgt acaggcagac	360
aagagcgttag cctgctgttg cctccatcac tatgaaatga cttatcttac ctgaaggacc	420
catggtttat gttccctctaa ttcccttcac tctccctaaag ccctctgaga gagatg	476

<210> 53
<211> 501
<212> DNA
<213> Homo Sapiens

<400> 53
gcctgtcgcc tcagatcgag gaatgcacatc tccgggacgt tgaaaacaca gacatgaagt 60
ataagaaccttgtacggagt cgtatctcca acctgaagga tgccaagaac cctgacctgc 120
ggcggaaatgt gctgtgtggg gccataaacac cccagcagat cgctgtatg acctcagagg 180
agatggccag tgatgagctg aaggagatcc gtaaggccat gaccaaggag gccatccgag 240
agcaccagat ggcccgcact ggcggcacgc agacagacat gttcacctgc ggcaagtgc 300
ggaaaaagaa ctgcacccatc acacaggtgc agacccgcag ctctgtatg cccatgcacca 360
cctttgttgt ctgcaacccatc tggggccccc tccccggccc acgtccctccg ttgacacacgc ttctctggag 420
tgtgctgcag ccttggggccc tccccggccc acgtccctccg ttgacacacgc ttctctggag 480
accctagaag gccccatgtc c . 501

<210> 54
<211> 453
<212> DNA
<213> Homo Sapiens

<400> 54
tggatgacat ctacaaggct gcggtagagc agctgacaga agagcagaaa aatgagttca 60
aggcagccctt cgacatcttc gtgctggcg ctgaggatgg ctgcacatcgc accaaggagc 120
tggcaaggt gatgaggatg ctggccaga accccacccc tgaggagctg caggagatga 180
tcgatgaggt ggacgaggac ggcagcggca cggtgactt tgatgagttc ctggcatgca 240
tggttcggtg catgaaggac gacagcaaag gaaatctga ggagctgtct gacctctcc 300
gcatgttga caaaaatgtt gatggctaca tcgacccatc tgagctgaag ataatgctgc 360
aggctacagg cgagaccatc acggaggacg acatcgagga gctcatgaag gacggagaca 420
agaacaacga cggccgcattc gactatgtc agt 453

<210> 55
<211> 498
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (142)..(142)
<223> n is a, c, g, or t

<400> 55
acccttggcc atcaggcgag gggctggcc tggcagctg gggcccttggc cagagtccac 60
tcccttcctg gctgtgtcac cccgagcagc tcatccacca tggaggatcat tggcctgagg 120
caagttcccc ggagagtcgg gntccctgt ggcccttca ggcctatgtc tgtgaggaag 180
gggcctgcc actctccca agagggctc catgttca ggtgcctcaa catggagct 240
tgcctggccct gggcttagggg cactgtctga actctgtact gtcaggataa actccgtggg 300
ggtacaggag cccagacaaa gcccaggccct gtcaagagac gcagaggccc cctgcaggg 360

ttggccccag ggacctggg acgaggctgc agaagcttc cctccctact ccctgggagc	420
cacgtgctgg ccatgtggcc agggacggca tgagcaggag gcggggacgt gggggcctc	480
tggtttggtg tcaacagc	498
<210> 56	
<211> 544	
<212> DNA	
<213> Homo Sapiens	
<400> 56	
gaagccacaa agatgccaca tggtagtata tcagttagag gtgactccac agtgcctct	60
ggagaagcaa tatgagtgc tgaagagtgg ggcctttgc tttgcctgg atataggggt	120
gctcttctac tgtaattggg tggaaaaaa ctctggcttt atggtattcc attaggttct	180
tttcatttaa agtagtctta aaatcaaagt atccaatatt taaaagccac aaagtagatt	240
acataaattag cagagattt agtcagtaaa atgtagaaaa tcaaactata agaaaattca	300
agtctttat ttgtgtctt gggatatgt cattattta aattccacac tcccttattt	360
aatcactttg gtaagtgcct ttgatgttt gaaatgtata gtgggagatg agcaaatgta	420
aatgtcatgt gcccgttcc ctgccttc aattccat aaccattttt accagtgttgc	480
caaagtttag acctttgtgt taatatcaga agtgtattt tagccccctcc atagtgaaca	540
atga	544
<210> 57	
<211> 535	
<212> DNA	
<213> Homo Sapiens	
<400> 57	
gccgaagaag cctgtctgtg ggggtgtcg cagcgctctg gcacctggcg tccgagccgt	60
ggagctcgag cggcagatcg agagcacaga gacttcttc catggctgcc gtaagaattt	120
cttcctgtcc aagatccggt cccacgtggc tacttgcattt aataaccaga attacatcat	180
ggaaggtgtg aaggccacca ttaaggatgc atctttcag ccaaggaatg tcccaaaccg	240
ttacaccttt cttgtctt actgtcctga gaagaacttt gatcaggaag gacttgcgg	300
acactgcaaa ttattccata gcacggatac caaatctgtg gtttgcctca tatgtgcctc	360
gatccccctgg ggagacccca actaccgcag cgccaaacttc agagagcaca tccagcgccg	420
gcaccggttt tcttatgaca cttttgttgc ttatgtgtt gatgaagagg acatgtgaa	480
tcaggggttg cagcgctcca tcatcgacca gtgagcagag tccgtgcctt ctatc	535
<210> 58	
<211> 479	
<212> DNA	
<213> Homo Sapiens	
<400> 58	
gctgaaagaa gcccacatag aactgcttag ggacagcacc actgactcca aagaaaatcc	60
cagcagaaag agaaatggaa tgtgcacgga tacacattca ctgctcagta agaggctcaa	120
gacatgactg atttgcatcc taaagcaaga tgcgatgtcc agagttacag agaatgagta	180

21

gatgtgtctc atcggttaat agctctatta tacctctaaa ggtggaaattt tcagtttaga	240
ttcataaaatg aaaaggtaaa tgagtaatca gaataaacca agtgataatc aaaccatgtc	300
aagattatta gttcagactc tagcctgtta attttcttag ttgatttctg aagctacctg	360
atttatttcta taaaattgtt agcttgc当地 ctcaaataa attggcagat ttacctctca	420
tgttttaatg tgtcaaatta gagagcaaag tataacaggt gccttcactt ttgagactt	479

<210> 59
<211> 518
<212> DNA
<213> Homo Sapiens

<400> 59 gtgccatagt gcaggcttgg ggagctttaa gcctcagtta tataacccac gaaaaacaga	60
. gcctcctaga tgtaacatc ctgatcaagg tacaattctt taaaattcac taatgattga	120
ggtccatatt tagtggtaact ctgaaattgg tcactttcct attacacgga gtgtgctaaa	180
actaaaaagc attttggaaac atacagaatg ttctattgtc attgggaaat ttttctttct	240
aaccaggctgg aggttagaaa gaagttatat tctggtagca aattaacttt acatccttt	300
tcctacttgt tatggttgtt tggaccgata agtgcgtta atcctgaggc aaagttagtga	360
atatgtttta tatgttatga agaaaagaat tggtaagt ttttattct actcttatat	420
gctggactgc attcacacat ggcataaaat aagtcaaggtt ctttacaaat ggtatgttga	480
tagatactgg attgtgtttt tgccatattt gtgcatt	518

<210> 60
<211> 489
<212> DNA
<213> Homo Sapiens

<400> 60 gggatgcatt tggccatt gttcaaagtg tcaagaacaa gcctctttc tttgccgaca	60
aactttacaa atccatgaag ggtgctggca cagatgagaa gactctgacc aggatcatgg	120
tatcccgcag tgagattgac ctgctcaaca tccggaggaa attcattgag aaatatgaca	180
agtctctcca ccaagccatt gagggtgaca cttccggaga cttcctgaag gccttgctgg	240
ctctctgtgg tggtgaggac tagggccaca gctttggcg gcacttctgc caagaaatgg	300
ttatcagcac cagccgccccat ggcataaggct gattgttcca gctccagaga ctaaggaagg	360
ggcaggggtg gggggagggg ttgggttggg ctcttatctt catggagctt agggaaacgct	420
cccaactccca cggccatcg agggccagca cggctgagcg gtaaaaacc gtagccatag	480
atcctgtcc	489

<210> 61
<211> 472
<212> DNA
<213> Homo Sapiens

<400> 61 atttcaaat ttctgcattc acggagaatg caaatatata gggcacctgg aagcagtaac	60
atgcaaatgt cagcaagaat attcgggtga acgggtgtgg gaaaagtcca tgaaaaactca	120
cagcatgatt gacagtagtt tatcaaaaat tgcattagca ggcatacgctg cctttatgtc	180

tgctgtgatc ctcacagctg ttgctgttat tacagtccag cttagaagac aatacgtcag	240
gaaatatgaa ggagaagctg aggaacgaaa gaaacttcga caagagaatg gaaatgtaca	300
tgctatagca taactgaaga taaaattaca ggatatcaca ttggagtcac tgccaagtca	360
tagccataaa tgatgagtcg gtccttttc cagtgatca taagacaatg gaccctttt	420
gttatgatgg ttttaaactt tcaattgtca cttttatgc tatttctgtta ta	472

<210> 62
<211> 523
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (41)..(41)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (440)..(440)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (442)..(442)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (485)..(486)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (488)..(491)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (493)..(498)
<223> n is a, c, g, or t

<400> 62	
gacaacagcc ctggagggga acagagttag agagatgttt ngctctggta cagcctgtgt	60
tgttgtccca gtttctgata tactgtacaa aggcgagaca atacacattc caactatgga	120
gaatggcct aagctggcaa gccgcattt gagcaaatta actgataatcc agtatggaaag	180
agaagagagc gactggacaa ttgtgctatc ctgaatggaa aatagaggat acaatggaaa	240
atagaggata ccaactgtat gctactggga cagactgttg catttgaatt gtgatagatt	300
tctttggcta cctgtgcata atgtagttt tagtatcaat gtgttacaag agtgattgtt	360
tcttcatgcc agagaaaatg aattgcaatc atcaaatggt gttcataac ttggtagtag	420
taacttacct taccttaccc anaaaaatat taatgtaaagc catataacat gggattttcc	480
tcaannannn nannnnnncc ttttgtactt cactcagata cta	523

<210> 63
<211> 373
<212> DNA
<213> Homo Sapiens

<400> 63		
gggcagatct tggactcatg aggaggggcc cccctgccc gagggtcaa cccttctgga	60	
aactgtgaag atctgacttc gccccccccc cccccatct tcgggaccag gatttgacaa	120	
gaagcacatg cacctaccca tacacccct cttctgagcg tccctgttcc cccatctcgc	180	
tccctccag gactctgacc ccagcattct caggcaccag tccctgtccg gaatgccacc	240	
cacatcttcc atttccatgt cccctccag agctggtggaa cccagggAAC agccactccc	300	
ctccactctc taccagataa ctgaggaggg gagaggtggg ccgtaacggg cacggatcac	360	
gatgtaaatt att	373	
<210> 64		
<211> 535		
<212> DNA		
<213> Homo Sapiens		
<400> 64		
agcttcagga cgctgtctgca gaggtggagc gactgagaag agaaaaccag gtcttaagcg	60	
tgagaatcgc ggacaagaag tactaccca gctcccagga ctccagctcc gctgcggcgc	120	
cccaagctgct gattgtgctg ctgggcctca gcgcgtctgc gcagttagat cccaggaagc	180	
tggcacatct tggaaagggtcc gtccctgtcg gcttttcgct tgaacattcc ctgtatctca	240	
tcagttctga gccccgtcatg gggcaacacg gttagccccgg agagcacggg gtagccggag	300	
aaggccctct ggagcaggto tggaggggcc atggggcagt cctgggtgtg gggacacagt	360	
cgggttgcacc caggcgtgtc tccctccaga gcctccctcc ggacaatgag tccccctct	420	
tgtctccac cctgagattt ggcattgggt ggggtgtggg gggcatgtgc tgcctgttgt	480	
tatgggtttt ttttgcgggg ggggttgctt ttttctgggg tttttagct ccaaa	535	
<210> 65		
<211> 452		
<212> DNA		
<213> Homo Sapiens		
<400> 65		
catgtggac cagatcaact cctgtctgga ccacctggag gagaagaatg accaccccca	60	
cgcggccctc caggagctgc tggagtccaa cggcagaca cgcctggagt tccagcagca	120	
gctcggggag gccccctgtg atgccagccc cttagctcca agagccccca accgggaccc	180	
aaccctgcct ccctgggcta ggctctggcc tgggactca cccctggct tagacacctt	240	
ctcaagggtt ggcatttcagg gacccctgggt gggctgtccat gcctggccca cccttcctgc	300	
ctgggcctcc cttggccata cttggccag ccccccaccc ctggcatgcc ctccctgggc	360	
caagagtggg cctgcaaccc acccaacttgc ctgcccaccc aactcctggg cgctccccac	420	
tctgcccagg ctttgagtgtt ccacattaaa tg	452	
<210> 66		
<211> 323		
<212> DNA		
<213> Homo Sapiens		
<400> 66		
cacttaccag tgagcatata tattttaaaa tactttttt ggatattgtt attcttaact	60	

ggttgtaaat tagaaaagct	gggattacat atggtgtgcg	gttacagtct aaatttttc	120
atcccttat gcatcataag	catgtttgtat atattttcaa	aaatagttct actgatgcta	180
caggaatttc aaggctgtgg	tgaatgttag tatttaccat	agggagtgaa gtggagttat	240
ggtttcattc aatagagtat	tgctgattat acttgagtgg	aatccttcc tcacgtactc	300
ccacagacgt ctgggcctgg	aaa		323

<210> 67
<211> 560
<212> DNA
<213> Homo Sapiens

<400> 67	ggcgaggag aacaaacaga	tcatccgcaa acacgcgcag	accttcgttg ccctctgtgc	60
cacagatgtg aagttcattt	ccaatccgcc cccatggtg	gcagcgggga gcgtgggtgc	120	
cgcagtgcaa ggcctgaacc	tgaggagccc caacaacttc	ctgtcctact accgcctcac	180	
acgcttcctc tccagagtga	tcaagtgtga cccggactgc	ctccgggcct gccaggagca	240	
gatcgaagcc ctgctggagt	caagcctgcg ccaggcccag	cagaacatgg accccaaggc	300	
cggcggaggag gaggaagagg	aggaggagga ggtggacctg	gcttgcacac ccaccgacgt	360	
gcgggacgtg gacatctgag	ggcgcaggc aggcgggcgc	caccgcacc cgcagcgagg	420	
gcggagccgg ccccaggtgc	tccctgaca gtccttcctc	tccggagcat tttgatacca	480	
gaagggaaag cttcattctc	cttgggtttt ctttgcgtct	ttcccccttc	540	
catctctgac ttaagaaaa			560	

<210> 68
<211> 471
<212> DNA
<213> Homo Sapiens

<400> 68	gttttggta tgtttaatct	gttatgtact agtgttctgt	ttgttattgt tttgttaatt	60
acaccataat gctaattaa	agagactcca aatctcaatg	aagccagctc acagtgcgt	120	
gtgccccgggt catctagcaa	gctgccgaac caaaagaatt	tgcacccgc tgccggccca	180	
cgtggttggg gccctgcct	ggcagggtca tcctgtgctc	ggaggccatc tcgggcacag	240	
ccccaccccg ccccacccct	ccagaacacg gctcacgcct	acctcaacca tcctggctgc	300	
ggcgtctgtc tgaaccacgc	gggggccttg agggacgctt	tgtctgtcgt gatggggcaa	360	
gggcacaagt cctggatgtt	gtgtgtatcg agaggccaaa	ggctggtggc aagtgcacgg	420	
ggcacagcgg agtctgtcct	gtgacgcgca agtctgaggg	tctggcggc g	471	

<210> 69
<211> 518
<212> DNA
<213> Homo Sapiens

<400> 69	aattcctgcc attctgggg	ttcttggagg aattcttgct	ttgtctaattc tgattctgct	60
gctcttgcgt	tttcttcgga ggagagcggt	ggtcaaagag cccttactgc	ccccagagga	120

25

tgacaccgg gacaacgtt	attactatga tgaagaagga ggccggagaag aggaccagga	180
ctttgacttg agccagctgc	acaggggcct ggacgctcgg cctgaagtga ctcgtaacga	240
cgttgcacca accctcatga	gtgtcccccg gtatcttccc cgccctgcca atcccgtatga	300
aattggaaat ttattatgtat	aaaatctgaa agcggctgtat actgacccca cagccccgcc	360
ttatgattct ctgctcgtgt	ttgactatga aggaagcggt tccgaagctg ctatgtctgag	420
ctccctgaac tcctcagagt	cagacaaaga ccaggactat gactacttga acgaatgggg	480
caatccgttc aagaagctgg	ctgacatgtatcgaggcg	518

<210> 70
<211> 182
<212> DNA
<213> Homo Sapiens

<400> 70	
cttttcaactg tggtggagtt ttctggagtg agcactcacg ccctaagcgc acattcatgt	60
gggcatttct tgcgagccctc gcagcctccg gaagctgtcg acttcatgac aagcattttg	120
tgaacttaggg aagctcaggg gggttactgg ctctcttga gtcacactgc tagcaaatgg	180
ca	182

<210> 71
<211> 538
<212> DNA
<213> Homo Sapiens

<400> 71	
tgaggagcca gcgcttaggg cagcagccgc ttcctagaag accaggtcat gatgatggc	60
agcgccccgag tggcgagct gctgctgtc cacggcgccg agcccaactg cgccgacccc	120
gccactctca cctgaccctgt gcacgacgt gcccgggagg gcttccttggaa cacgctggtg	180
gtgctgcacc gggccggggc gcccgtggac gtgcgcgtatg cctggggccg tctgcccgtg	240
gacctggctg aggagctggg ccatcgcgat gtcgcacggt acctgcgcgc ggctgcgggg	300
ggcaccagag gcagtaacca tgcccgata gatgccacgg aaggccctc agacatcccc	360
gattgaaaga accagagagg ctctgagaaa cctcgggaaa cttagatcat cagtcaccga	420
aggtcctaca gggccacaac tgccccggcc acaacccacc ccgccttcgt agttttcatt	480
tagaaaaatag agctttaaa aatgtccctgc cttaaacgt agatatatgc ttcccccc	538

<210> 72
<211> 513
<212> DNA
<213> Homo Sapiens

<400> 72	
atatttagtta ccctgggtgtg ctgtatttctc taaaaccttt aaatgtttgc atgcagccat	60
tcgtcaaatg tcaaataattc tctctttggc tggaatgaca aaaactcaaa taaatgtatg	120
attaggagga catcataacc tatgaatgtat ggaagtccaa aatgtatggta actgacagta	180
gtgttaatgc cttatgttta gtcaaactct catttaggtg acagcctgggt gactccagaa	240
tggagccagt catgctaaat gccatataact cacactgaaa catgaggaag caggtagatc	300
ccagaacaga caaaaacttccatctaaacat gagagtccag gctgtctgag tcagcacagt	360

aagaaaagtcc	tttctgcttt	aactcttaga	aaaaagtaat	atgaagtatt	ctgaaattaa	420
ccaatcagtt	tattnaaatc	aatttattta	tattcttctg	ttcctggatt	cccattttac	480
aaaacccact	gttctactgt	tgtattgcc	agt			513

<210> 73
<211> 530
<212> DNA
<213> Homo Sapiens

<400> 73	ggatttgtgt	tcttacagta	cttgaaaata	tttaaggaag	agatgaagct	ctgcagttt	60
	ttctatgtgg	gatgattact	tttttaagga	ggattaattc	tgaggttagta	tagtaactaa	120
	aggggaatat	atgaattgtt	taacaaat	taa	gaatttgtt	acaactactt	180
	attatgtcaa	aacttacatt	acttgccaa	gagtatgtg	ttataggaaa	cataaataaag	240
	attacagagg	tatcaattt	gttaaaattc	accatttt	aagactaagc	aataatctt	300
	acaacctctt	tcctgaatat	ttaaatgtgt	ttgtatggtg	ttatgactaa	ttgttactga	360
	tttagagact	aagccctctt	aaaaccttta	gttaaatata	aaaagaaaatt	atataatatct	420
	tgcctccctg	atggaaaact	atataaaatt	gtagacttaa	aaggtttgt	gaaaatacatt	480
	aggatatacg	aaaactaaat	atatggagtt	gttttatgac	tattacatgt		530

<210> 74
<211> 406
<212> DNA
<213> Homo Sapiens

<400> 74	ggctgcctgc	ggatgaagga	ccagtgtgac	aagtgcgggg	agatcttgtc	tgtggactgt	60
	tccaccaaca	accctccca	ggctaagctg	cggcgggagc	tcgacgaatc	cctccaggtc	120
	gctgagaggt	tgaccaggaa	atataacgag	ctgctaaagt	cctaccagt	gaagatgctc	180
	aacacctcct	ccttgctgga	gcagctgaac	gagcagttt	actgggtgtc	ccggctggca	240
	aacctcacgc	aaggcgaaga	ccagtaactat	ctgcgggtca	ccacgggtgc	tccccacact	300
	tctgactcgg	acgttccttc	cggtgtca	gaggtggtgc	tgaagctctt	tgactctgat	360
	cccatcactg	tgacggtccc	tgtagaagtc	tccaggaaga	acccta		406

<210> 75
<211> 286
<212> DNA
<213> Homo Sapiens

<400> 75	agcagctgaa	cgagcagttt	aactgggtgt	cccgctggc	aaacctcacg	caaggcgaag	60
	accagtacta	tctgccccgt	accacgggtgg	cttcccacac	ttctgactcg	gacgttcctt	120
	ccgggtgtcac	tgaggtggtc	gtgaagctct	ttgactctga	tcccatcact	gtgacggtcc	180
	ctgtagaagt	ctccaggaag	aaccctaaat	ttatggagac	cgtggcggag	aaagcgctgc	240
	aggaataccg	caaaaagcac	cgggaggagt	gagatgtgga	tgttgc		286

<210> 76

<211> 436
<212> DNA
<213> Homo Sapiens

<400> 76
gaaaagactgt gctgtccttt aacatagggtt tttaaagact aggatattga atgtgaaaca 60
tccgttttca ttgttcactt ctaaacccaaa aattatgtgt tgccaaaacc aaacccaggt 120
tcatgaatat ggtgtctatt atagtgaaac atgtactttg agcttattgt ttttattctg 180
tattaaatat ttccagggtt ttaaacacta atcacaaact gaatgacttg acttcaaaag 240
caacaacctt aaaggccgtc atttcatttag tattcctcat tctgcacccct ggcttggaaa 300
acagctctgt tgaatcacag tatcagtatt ttcacacgta agcacattcg ggccatttcc 360
gtggtttctc atgagctgtg ttccacagacc tcagcaggc atcgcatttgc ccgcaggagg 420
gcagattcgg accact 436

<210> 77
<211> 429
<212> DNA
<213> Homo Sapiens

<400> 77
tcggctactc ttttgtatg cacaccagcg ctgggtcaga aggctctggc caagccctgg 60
cgccccccgg ctccctgcctg gaggagtta gaagtgcgcc attcatcgag tgtcacggcc 120
gtgggacctg caattactac gcaaacgctt acagctttg gctgccacc atagagagga 180
gcgagatgtt caagaaggct acgcccgtcca ctttgaaggc aggggagctg cgacgcacg 240
tcagccgctg ccaagtctgt atgagaagaa cataatgaag cctgactcg ctaatgtcac 300
aacatggtgc tacttcttct tctttttgtt aacagcaacg aacccttagaa atatatccctg 360
tgtacccacat tgcataat gaaaaccgta aagtgcctt taggaatttgc cgtactaac 420
acaccctgc 429

<210> 78
<211> 195
<212> DNA
<213> Homo Sapiens

<400> 78
tccccctgtta gactagtgcc gtgggagttac ctgtgtccca gctgctgtgg cccctccgt 60
gatccatcca tctccaggga gcaagacaga gacgcaggat ggaaagcggg gttectaaca 120
ggatgaaagt tccccatca gtccccccag tacctccaaag caagtagctt tccacatttg 180
tcacagaaat cagag 195

<210> 79
<211> 301
<212> DNA
<213> Homo Sapiens

<400> 79
tgggtgtggg agcccttgg agaacgcccag tctccaggta cccctgcattc tatcgagttt 60
gcaatgtcac aacctctctg atcttgcgtc cagcatgatt cttaataga agttttat 120
ttcgtgcact ctgctaatca tgggggttag ccagtgaaac agcgggagcc tggctgggtt 180

28

tgccagattgc ctcctaata	cgccggctaa aaggaaacca agtggtcagg agttgttct	240
gaccactga tctctactac	cacaaggaaa atagtttagg agaaaccagc ttttactgtt	300
t		301

<210> 80
<211> 459
<212> DNA
<213> Homo Sapiens

<220>		
<221> misc_feature		
<222> (164)..(164)		
<223> n is a, c, g, or t		
<400> 80		
ggaaacgttc ccagttcatt ttca	ttcagtctg ttgtgagcac agttctgaag ggtttattat	60
tgtcaaaata agttttgttt tg	ttttgtttt atgttgggtt ttatgttg tctttgacc	120
cttaatgctc aggttcttgc	gggagttaat cagccacatc caangttacc ttgaggggga	180
agaagagggt gatgctcaga	agctaaacaa gacaggggcc acatgaccct ctattgatta	240
cccccaagta gaaagtctg	tggtttatg ttatgttata atagttgatc atatatggca	300
taattttcta tcagttcct	actcagtcac tataaacaca gacttgaat agtactttaa	360
atgtccaaat acctaaatgt	gctaaactgg aggtaactat ttcttaggtt tagttaat	420
gaaagtcatg atcagccaca	caactgtttt gtacataact	459

<210> 81
<211> 394
<212> DNA
<213> Homo Sapiens

<400> 81		
aatc	tttattttt gttcagagtt gtttgggggt tctgtttcag agcataaaac ctaaaggta	60
tagtagaaca	aggcaccttc taaaagaaa tcttgcttca gaccatcagt tacagagaat	120
ttcctaaagt	aaaattgaag caactacaac ttctccttag acactttgga atctaaccac	180
ttaaggacct	ttttaaagag atagcttctc ttcttctga agatcaattt ctccaaggc	240
caagattgtc	cttttctccc atttcttgct agctattgca aatgaggaa gaacattatt	300
catctcttct	cccccccccc ttctgattct ttcttcttca agttttgttc ctgggttcaa	360
gtagtattac	caccctttca caagcaacag actc	394

<210> 82
<211> 514
<212> DNA
<213> Homo Sapiens

<220>		
<221> misc_feature		
<222> (89)..(89)		
<223> n is a, c, g, or t		
<400> 82		
gctcaactaca	ctattcattt cacacaatg aattttcac tttaagat gcattttgg	60
tgctcaaaacc	agatcgaagt ttgtctctna aagctattgt ctgcacaggc tgctgcattc	120

tctgttgtta	aatggatgga	caggctattc	taaattttgg	ttgatacttt	tgctactatg	180
ggcaattaac	ttgaaaaaaaaa	taatcgatcc	caactctgtg	ctctgatgta	cctcttctgc	240
ccctttatg	acaccttga	ccaaatgcct	tctatggttc	acagtgcagg	cacaaaacta	300
cctctgatac	agaaggttct	ttacaagctt	atttacata	ccgtgaatcc	ctcacctaaa	360
gggagaggta	aaagcaaaga	ctgcttga	tgggtattga	gggagattgt	gtccatacca	420
agccaccctg	aagaagtatt	tcacttgcag	tagaactgtg	gatttgtgct	gtcatttcac	480
cttggaaataa	acacctatct	ctaaggcagga	ccaa			514
<210>	83					
<211>	299					
<212>	DNA					
<213>	Homo Sapiens					
<400>	83					
caccaaatta	cctaggctga	ggttagagag	attggccagc	aaaaactgtg	ggaagatgaa	60
ctttgtcatt	atgatttcat	tatcacatga	ttatagaagg	ctgtcttagt	gcaaaaaaca	120
tacttacatt	tcagacatat	ccaaaggaa	tactcacatt	ttgttaagaa	gttgaactat	180
gactggagta	aaccatgtat	toccttatct	tttactttt	ttctgtgaca	tttatgtctc	240
atgtaatttg	cattactctg	gtggattgtt	ctagtactgt	attgggcttc	ttcgtaat	299
<210>	84					
<211>	219					
<212>	DNA					
<213>	Homo Sapiens					
<400>	84					
ttatcgccct	gagaagatct	accccaggga	aatctgaga	catcttgccct	acttttctt	60
attagcttcc	tcctcatcca	tttctttat	accttcctt	tttggggagt	tgttatgcca	120
tgattttgg	tatttatgta	aaaggattat	tactaattct	atttctctat	gtttattcta	180
gttaaggaaa	tgttgagggc	aagccaccaa	attacctag			219
<210>	85					
<211>	518					
<212>	DNA					
<213>	Homo Sapiens					
<220>						
<221>	misc_feature					
<222>	(61)..(65)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(71)..(71)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(73)..(73)					
<223>	n is a, c, g, or t					
<220>						
<221>	misc_feature					
<222>	(112)..(112)					

<223> n is a, c, g, or t

<220>

<221> misc_feature

<222> (163)..(163)

<223> n is a, c, g, or t

<220>

<221> misc_feature

<222> (295)..(295)

<223> n is a, c, g, or t

<400> 85

aaggactggt atcttttgt gagcaataag gactggataa agactgcata tccttggtc	60
nnnnncagca ncataacaat aaggagggtt ttaatgtgaa gcaggcaatc tnccagcccc	120
ttctggtctt ggatgaaata gttcacaga gtattgcacc aanaatacac aatggaggct	180
gaaaagttca acatatttttta agtcaattaa tcaaattgca ttgattctt atgctttctt	240
agaggcctac atgatttctt agattgcctt gataaactat cataagggtt ccacntcccc	300
tcattagct ccccccaggga tttctttcc cccatgtcat acacccagtc ctaaatcaac	360
ccccaggct atccttccat cccttctgca gagggactt ttgtcagact ctgcaacaaa	420
c当地tagctc tatccagagt gtctctgct gctaagattt gtatcttctt cctcaaaagc	480
ctggatggtg aatgggggtg cattagtcag aattctcc	518

<210> 86

<211> 458

<212> DNA

<213> Homo Sapiens

<400> 86

taaaaaacctg tatctgaccc actttgtat ttttgctcca atatccattc tgttagacttt	60
tgaaaaaaaaa gtttttaatt tgatgccaa tatattctga cctttaaaaa attcttggtc	120
atatgggaga agggggagta atgacttgc caaacagttt ttctggtgta tattttatgt	180
tttttaaaaa gagtaatttc atttaaatat ctgttattca aatttgatga tttttttatgt	240
aatataatgt attttttttt tattttgcac tctgtatggc cactttttaa gtttgaagag	300
ccattttgtt aaacggtttt tattaaagat gctatggAAC ataaagggtt attgcattgca	360
atttaaagta acttatttgc ctatgaatat tatcggttta ctgttattgtt tcaattttttt	420
tgtttcaat atcagcttttataattgtt accttaag	458

<210> 87

<211> 336

<212> DNA

<213> Homo Sapiens

<400> 87

gggatccat ttagctctta gtaccactaa tcaaaaggatc ggcattgtgc tcatgtatctt	60
tgctgtttctt atgtcggttggaa agcaccggat gggggtagtg agcaatctg ccctgctcag	120
cagtcaccat agcagctgac tgaaaatcg cactgcctga gtatgttttttgc tcaatgttac	180
ttgaatctact aactgactga aaattgaatg ggcaataag tgctttgtc tccagatgtt	240
gcgggagacc cttccaccc aagatggata tttcttcccc aaggatttca agatgaatttgc	300
aaatttttaa tcaagatgtt gtgttattt ctgttg	336

<210> 88
<211> 521
<212> DNA
<213> Homo Sapiens

<400> 88
atatcttctt caggctctga caggcctcct ggaaacttcc acatattttt caactgcagt 60
ataaagtcag aaaataaaagt taacataact ttcactaaca cacacatatg tagatttcac 120
aaaatccacc tataattggt caaaagtgggt gagaatatat ttttttagtaa ttgcattcaa 180
aattttctta gcttccatcc tttctccctc gtttcttctt tttttggggg agctggtaac 240
tgatgaaatc ttttcccacc ttttcttcc aggaaatata agtgggtttg tttggtaac 300
gtgatacatt ctgttatgaat gaaacattgg agggaaacat ctactgaatt tctgttaattt 360
aaaatatttt gctgctagtt aactatgaac agatagaaga atcttacaga tgctgctata 420
aataagtaga aaatataaaat ttcatcacta aaatatgcta ttttaaaatc tatttcctat 480
attgtatttc taatcagatg tattactctt attatttctta t 521

<210> 89
<211> 503
<212> DNA
<213> Homo Sapiens

<400> 89
gtggctatcc actgttagtt cagaagctgg gcttggacta ctcttatgat ttagctccac 60
gagccaaaat tttccggcg gaccaaggga aagtgactga tacggcatcc atgaaatata 120
tcatgcata caacaattat aagaaggatc cttacagtag aggtgacccc tgtaatacc 180
tctgctgccg tgaggacctg aactcaccta acccaagtcc tggaggttgt tatgacacaa 240
aggtggcaga tatctaccta gcatctcagt acacatccta tgccataagt ggtccccacag 300
tacaaggtgg cctccctgtt tttcgctggg accgtttcaa caaaactcta catcaggcga 360
tgccagaggt ctacaacttt gattttatta ccatgaaacc aattttgaaa cttgatataa 420
aatgaaggag ggagatgacg gactagaaga ctgtaaataa gataccaaag gcactatTTT 480
agctatgttt ttcccatcag aat 503

<210> 90
<211> 275
<212> DNA
<213> Homo Sapiens

<400> 90
ccccatcacg gagggtccag actgtccact cgggggtggg gtgagactga ctgcaagccc 60
caccctcctt gagactggag ctgagcgtct gcatacgaga gacttgggtt aaacttggtt 120
ggtccttgc tgcaccctcg acaagaccac accttggac ttgggagctg gggctgaagt 180
tgctctgtac ccatgaactc ccagttgcg aattaataag agacaatcta ttttgttact 240
tgcacttgtt attcgaacca ctgagagcga gatgg 275

<210> 91
<211> 405
<212> DNA

<213> Homo Sapiens

<400> 91
 tcatctgatg tttctatagt cactttgcca gctcaaaaga aaacaatacc ctatgttagtt 60
 gtggaaagttt atgctaataat tgtgttaactg atattaaacc taaaatgttct gcctaccctg 120
 ttggtataaa gatattttga gcagactgta aacaagaaaa aaaaaatcat gcattcttag 180
 caaaattgcc tagtatgtta atttgctcaa aatacaatgt ttgatTTTat gcactttgtc 240
 gctattaaaca tcctttttt catgttagatt tcaataattg agtaatttttta gaagcattat 300
 ttttaggaata tatagttgtc acagtaaata tcttggTTTt tctatgtaca ttgtacaaat 360
 ttttcattcc ttttgctctt tgtggTTGGA tctaacaacta actgt 405

<210> 92
 <211> 375
 <212> DNA
 <213> Homo Sapiens

<400> 92
 aagctatgtg tatcttctgt gtaaaagcagt ggcttcactg gaaaaatgggt gtggctagca 60
 tttccctttg agtcatgatg acagatggtg tgaaaaccat ctaagttgc ttttgaccat 120
 caccccccag tagcaatttg ctttcataat ccatttagca atccaggcct ctgttgaAAA 180
 gataatatga gggagaaggg aacacatttc cttctgaact tactcccta agtcactttc 240
 cttatgtatc atctaataca atgatggttg agtggAAata cagaaggGGgt gtttgagttat 300
 tcagatttca taaaacactt ctttggaaata tagctgcatt aacttggaaa gaaggctgtt 360
 gggccagaag acaga 375

<210> 93
 <211> 533
 <212> DNA
 <213> Homo Sapiens

<400> 93
 gctgggtgt gtgtcaaaacc ctcactcacc cacgcactca cacacagcat tctgttctcc 60
 atgcaaagtt aagatcgaat ccatccgctt gttagggAAA aaaaggAAAA aaattaacca 120
 gagagggtct gtaatctcgC agagcacagg cagaatcgTT cttccTTgc tgcatttct 180
 ctttagacta atagacgttt tggaaagtTC ggctagtgtt cgtgtgtttg tcgttagcacc 240
 cagagcetcc accaaaccct ctccatgtct ttaccccca gtcgctctaa gatctgcttg 300
 aagtctcgta tttgtactgc tttctgcTT tctcccaacc ctcctagcac ccccacatcc 360
 cccatcttagt aacatctcag aaatttcATC cagaggaaca aaaaattaa aaatagaaca 420
 tagcaaagca aagacagaat gcccccccccc aaatattgtc ctgtccctgt ctgggagttg 480
 tgttatTTaa agatattctg tatgttgtat ctTTTgcATG tagttccTT aat 533

<210> 94
 <211> 413
 <212> DNA
 <213> Homo Sapiens

<400> 94
 atctggaagg ctctgatcca cctgagcgac ctccgggagt acaggcgctt tgagaaggag 60

33

aagctcaagt cccagtggaa caatgataat cccctttca agagcgccac cacgacggtc	120
atgaaccca agtttgctga gagtttaggag cacttggta agacaaggcc gtcaggaccc	180
accatgtctg ccccatcacg cggccgagac atggcttggc cacagcttt gaggatgtca	240
ccaattaacc agaaatccag ttatttccg ccctaaaaat gacagccatg gccggccggt	300
gcttctgggg gctcgctggg gggacagctc cactctgact ggcacagtct ttgcattggag	360
actttagggag ggcttgaggt tggtgaggtt aggtgcgtgt ttccctgtgca agt	413

<210> 95
<211> 465
<212> DNA
<213> Homo Sapiens

<400> 95 cagccggcc agttggagtt gtagtaccac gagggacgcc aactcccaga ggagtcctgt	60
ccacccgagg gccagtgagt cgggaaagag gacttctcac tcggcagagca agaggagtc	120
ccccaaactgg gtacagaccc ccaccgcccac ccccgacaca agagacttat ggagaatatg	180
actatgatga tggatatggc actgctttagt atgaacagag ttatgattcc tatgataaca	240
gctatagcac cccagcccaa agtggtgctg attactatga ttacggacat ggactcagtg	300
aggagactta tgattcctac gggcaagaag agtggactaa ctcaagacac aaggcacctt	360
cagcaggagac agcaaaggc gtctacagag accagccata tggcagatac tgattgtact	420
gtctgatgtt gtgaaatagc caatctccac cagtcctgta tactg	465

<210> 96
<211> 537
<212> DNA
<213> Homo Sapiens

<400> 96 gagaacacgg tggcagagac ggagtgcgc tatgcctgc agctgcagca gatccaggg	60
ctcatcagca gcatcgaggg ccagctgagc gagctccgca gtgagatgga gtgccagaac	120
caagagtaca agatgctgct ggacatcaag acacgtctgg agcaggagat cgccacctac	180
cgcagcctgc tcgaggccca ggacgccaag aagcgtcage cccctgtac cctctgttac	240
cacgacttct agtgcctctg ttaccaccac ctctaattgc tctggcgcc gcacttctga	300
tgtccgtagg ccttaaatct gcctggcgctc ccctccctct gtcttcagca cccagaggag	360
gagagagccg gcagttccct gcaggagaga ggagggctg ctggacccaa ggctcagtc	420
ctctgctctc aggacccctt gtcctgactc tctctgtatg gtggccctc tgtgtcttc	480
tcttcggtc ggatctctct cctctctgac ctggatacgc ttgggttct caacttc	537

<210> 97
<211> 372
<212> DNA
<213> Homo Sapiens

<400> 97 aactttaact tagagttca ttactttaag aatggaaaac aacctctgag tttgatttcc	60
caaagtttca taaagccccct aagctcatga ttttcatcaa ctctttgccc acatagtc	120
ttacctccac agccgttgt tgcataaaaa ggggtgggtt gttttggatt tgat	180

caacttgcag tgagaaatag gatagggtgac aaaaccttac ttgtttctt aagacaattc 240
 agtgcttgcg catctctgtc agaaaatggaa tggataactg ttagccaatt agaattat 300
 tatgtattgt tattgtgtt tgctgatttt tataatgaaaa tataattatt catttttgat 360
 ctctggaaagc aa 372

<210> 98
 <211> 365
 <212> DNA
 <213> Homo Sapiens

<400> 98
 gggagccaaag gctttatacg tctaaagaaa atattcaga gctgaatccg cccagtgata 60
 gcctgtgggc accagcagca agggctgcc a tgggatacag cacccatcta caaagacctc 120
 tattacataa acactgcttc ttacaggaaa caaacctttt ctggatctc cttttgtgaa 180
 aaccagttt aatgtgctaaa agtaaaaaatg ctatcccgtt gtgtggtctt gttcagaagc 240
 agccagattt ccaatgttgt tttccccctc cactcagaaa cccctgcctt ttcccttcag 300
 aaaaacgatgg caggcattcc tctgagtttca caagcagaga ctcactccaa cccaaacttag 360
 ctggg 365

<210> 99
 <211> 465
 <212> DNA
 <213> Homo Sapiens

<220>
 <221> misc_feature
 <222> (110)..(110)
 <223> n is a, c, g, or t

<400> 99
 acacacacat gcaatttgc ttaacaaaag tattttataa tacagttca tacagaatta 60
 ccttaaaagg gagtctttag tttcaacta cagatagttg taagggatcn tacagaagat 120
 attgatgata gttgaaatat tcttagaagg ggtgtgtatg tctagctgtg tctaccatgt 180
 gtatgtattc ttgacaagca gtataaaaata cctgtgattt ttctttacat tagggataat 240
 gcataaggaa ttaatcttca tatatattat catccctaat gtagcagggg gaagtattta 300
 attggccatg atatgtatTT tacttataact atgccagaga ggaaactata aagtaattac 360
 acatgtataatc ttgggtttt cacatatgtt ggttattttt ttgagtaggt tgaagaagaa 420
 aaaaatatt taaatgtattt gattttttttt gatgtttttt tcaat 465

<210> 100
 <211> 515
 <212> DNA
 <213> Homo Sapiens

<400> 100
 gaactctgca ttcatgggt ttacagaaat tggtgcaggc agccagcagt tagattccat 60
 tcattgttaca cagttggaga gagataccgt ttttagtgtgt ttagacaaat ttgtgaaaat 120
 tggataatcta caagggaaat taaaatcaag taagaaaactg gctctgagt taagtttga 180

35

ttttcgatt	aatctgttag	tatgccttc	agacagtgt	ttggcttct	ggaaacatgg	240
gatgcagggt	aaaagcttca	agtcagatga	ggttaccag	gagatttcag	atgaaacaag	300
agtttccgc	ttatttaggat	cagacagggt	tgtcgtttg	gaaagtaggc	caacagaaaa	360
tcctactgca	cacagcaatc	tctacatctt	ggctggacat	gaaaatagtt	actaagcaac	420
agaaactgat	ctcaaatacgac	aggaaaatga	atatactcca	ttgaaaggga	aaataaggaa	480
attcaataca	aactgcacta	tgatttgctt	taact			515

<210> 101

<211> 525

<212> DNA

<213> Homo Sapiens

<400> 101	ctcagagcca	cccctaaaga	gatccttga	tatttcaac	gcagccctgc	tttgggctgc	60
cctggtgctg	ccacacttca	ggctcttctc	cttcacaac	cttctgtggc	tcacagaacc		120
cttggagcca	atggagactg	tctcaagagg	gcactggtgg	cccgacagcc	tggcacaggg		180
cagtggacca	gggcatggcc	aggtggcac	tccagacccc	tggctttca	ctgctggctg		240
ccttagaacc	tttcttacat	tagcagttt	ctttgtatgc	actttgtttt	tttctttggg		300
tcttgtttt	ttttccact	tagaaattgc	atttcctgac	agaaggactc	aggttgtctg		360
aagtcaactgc	acagtgcato	tcagcccaca	tagtcatgg	tcccctgttc	actctactta		420
gcatgtccct	accgagtctc	ttctccactg	gatggaggaa	aaccaagccg	tggcttcccc		480
ctcagccctc	cctgccccctc	ccttcaacca	ttcccccattgg	gaaat			525

<210> 102

<211> 418

<212> DNA

<213> Homo Sapiens

<400> 102	gcaacaaccg	aaaatgcacc	agccccaggt	cctcgacac	cgaggagaat	gtcaagaggc	60
gaacacacaa	cgtcttggag	cgccagagga	ggaacgagct	aaaacgggac	tttttgccc		120
tgcgtgacca	gatcccgag	ttggaaaaca	atgaaaaggc	ccccaaaggta	gttatcccta		180
aaaaagccac	agcatacatc	ctgtccgtcc	aagcagagga	gcaaaagctc	atttctgaag		240
aggacttgtt	gccccaaacga	cgagaacagt	tgaaaacacaa	acttgaacag	ctacggact		300
cttgcgtta	aggaaaagta	aggaaaacga	ttccttctaa	cagaaatgtc	ctgagcaatc		360
acctatgaac	ttgtttcaaa	tgcattatca	aatgcacact	cacaacccctg	gctgagtc		418

<210> 103

<211> 462

<212> DNA

<213> Homo Sapiens

<400> 103	aacatccgcc	ttgttaaccag	tgcgtctggc	ttggcacttc	cacccgcacc	tcattcctac	60
atcaatgagt	ggctccaaat	agacctgggg	gaggagaaga	tctgtgggg	catcatcatt		120
cagggtgaaa	agcacccgaga	gaacaagggt	ttcatggaga	agttcaagat	cgggtacagc		180
aacaacggct	cgactggaa	gatgatcatg	gatgacagca	aacgcaaggc	gaagtcttt		240

gaggggcaaca acaactatga tacacctgag ctgcggactt ttccagctct ctccacgcga	300
ttcatcagga tctaccccgaa gagagccact catggcggac tggggctcag aatggagctg	360
ctgggctgtg aagtggaaac ccctacagct ggaccgacca ctcggaaacgg gaacttggtg	420
gatgaatgtg atgacgacca ggccaactgc cacagtggaa ca	462

<210> 104
<211> 370
<212> DNA
<213> Homo Sapiens

<220>	
<221> misc_feature	
<222> (168)..(168)	
<223> n is a, c, g, or t	
<400> 104	
gcaaataatct taccaggcag cctatgaatt aacccaaaga agctttggtt ggaaaaatgg	60
gatttttatac atgccatgtt ggacatgaga ttttttagat cttccttccc acattgctag	120
acgtctcaact caaagacatt tggggaggat cacatttgcatacataganga gacagtccat	180
tcatcttagt taaaattggat tgagaatgcc ttttggggaggat tggggggggat tggggggggat	240
gaaagaagaa tagtttttg tccccagaga cattcattta gttgatataa tcctaccaga	300
aggaaagcac taagaaaacac tggggggggat ttttggggggat caacagactt aaagttgtcc	360
tcagcccaagg	370

<210> 105
<211> 434
<212> DNA
<213> Homo Sapiens

<400> 105	
caggtgtatac tgcacagtgg tggccccaca gcagaccatg tggtcacggg atggccgcac	60
aaaacagctg aggccatgtac tggagaaggt gcagaacatg tctcaatcca tagaggctt	120
ggacaggcgg acccagagag acttgcagta cgtggagaag atggagaacc aaatgaaagg	180
actggagtcc aagttcaaacc aggtggagga gagtataag caacacctgg ccaggcagtt	240
taagggctaa cttaaaagag tttttcaat gctgcagtga ctgaagaagg agtccactcc	300
catgttaacca tgaaagagag ccagagact ttttgcacca tgcattttta ctattattt	360
ccaaatactta gcaccatttc actaaggaac cttgaataca accaggatcc tcctttgcat	420
gcgactgttag ctgc	434

<210> 106
<211> 503
<212> DNA
<213> Homo Sapiens

<220>

<221> misc_feature

<222> (158)..(158)

<223> n is a, c, g, or t

<220>

```

<221> misc_feature
<222> (216)..(217)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (231)..(231)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (250)..(250)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (261)..(261)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (291)..(291)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (297)..(297)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (341)..(341)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (352)..(352)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (365)..(365)
<223> n is a, c, g, or t

<400> 106
gcggccaca gacgtcgaa gaaactccg tattgcagc tggaactgca gcccacggcg      60
ccccggttt cctcccccgc ctgtccctct ctggtaaac aacataactaa agaggcgagg      120
caatgactgt tggccagttc tcaccgggaa aaaacccnac tgtaggatg gcatgaacat      180
ttcccttagat cgtggtcagc tccgaggaat gtggcncca ggctcttga ngagccatgg      240
gctgcacccn ggccgttaggc nttagttaac tcgcataccca ttgcagtgcc ngtttcnttg      300
actgtgttgc tgtctcttag attaaccgtg ctgaggctcc nacatagctc cntggacctg      360
tgtcnttagta catactgaag cgatggtcag agtgtgtaga gtgaagttgc tgtgcccaca      420
ttgtttgaac tcgcgtaccc cgtagataca ttgtgcaacg ttcttctgtt attcccttga      480
ggtggtaact tcgtatgttc agt                                         503

<210> 107
<211> 556
<212> DNA
<213> Homo Sapiens

<400> 107
ggagacttga gcttgaccta aggatatgca ttaaccactc tacagactcc cactcagtac      60

```

38

tgtacagggt ggctgtggc ctagaagttc agttttact gaggaaatat ttccattaaac	120
agcaattatt atattgaagg cttaataaaa ggccacagga gacattacta tagcatagat	180
tgtcaaatgt aaatttactg agcgtgtttt ataaaaaact cacaggtgtt tgaggccaa	240
acagattttt gacttacctt gaacggataa gaatctatag ttcactgaca cagtaaaatt	300
aactctgtgg gtgggggcgg gggcatagc tctaatactaa tatataaaaat gtgtgatgaa	360
tcaacaagat ttccacaatt cttctgtcaa gcttactaca gtgaaagaat gggattggca	420
agtaacttct gacttactgt cagttgtact tctgtccat agacatcagt attctgccat	480
cattttgtat gactacctca gaacataaaa aggaacgtat atcacataat tccagtcaca	540
gttttggtt cctctt	556

<210> 108
<211> 543
<212> DNA
<213> Homo Sapiens

ctgacctctt tgaagttgca gaatgctttg aaattctaát ggtatctgaa atatcagctc	60
atagaaagta acaaaaatttg ctgtcacctt aaataagaca ttttaatttt gttataatgt	120
acaattttaga agtttgatta attatattat ctattnaggc attaatataa aagaggtagg	180
agtctgttat ttaaaaaaaag cattaaattt aaaaaaaaaac tgtcttgtct acttttagct	240
tcattctccc atatttgaa gggtgtgtaa cttagctct gcaggattgc atggggtaaa	300
acttggtagg aacacatgtg aaccattgct acattgttagg ttgtgatcat tttgccccac	360
tgaagcccat gatatctgacc ttacgtgcct tttgaacttag gagaatcgaa ctaatttatt	420
aatgtatgata attataatgt atctgtacag cacttttac atttgcgaag tgctttccaa	480
tccatgttag ttacttagtta ttacagctgt aaggataaaa cacgtcatgt ggattcattt	540
tga	543

<210> 109
<211> 458
<212> DNA
<213> Homo Sapiens

agaaaatttg ccaatcttc ctactttcta ttttatgtat gacaatcaaa gccggcctga	60
gaaacactat ttgtgacttt ttaaacgatt agtgtatgtcc ttaaaaatgtg gtctgccat	120
ctgtacaaaa tggccctatt tttgtgaaga gggacataag ataaaatgtat gttatacatc	180
aatatgtata tatgtatccc tatatagact tggagaatac tgccaaaaca tttatgacaa	240
gctgtatcac tgccttcgtt tatattttt taactgtgtat aatccccaca ggcacattaa	300
ctgttgact tttgaatgtc caaaaatttat atttttagaaa taataaaaag aaagataactt	360
acatgttccc aaaacaatgg tgggtgaat gtgtgagaaa aactaacttg atagggtctaa	420
ccaataaaaa atgtattacg aatgccccctg ttcatgtt	458

<210> 110
<211> 412
<212> DNA

<213> Homo Sapiens

<400> 110
gtcaaacat gactcgacata tggcaaaaga acggccac agtacagcct cacattttc 60
ttccaaattct gaagatacag agatgtgatg aaaacaagta atagctttgg ctgtttattt 120
gatacgcttt tctgggtatt taataggaat ccttcctcaa ggaatgagtt gtgacctgtt 180
tactgtctct tttagaagaaa aactccactg gaaaccatc accatgtgtg actgtttct 240
gttatcattt gtcttacagg cggttattgc agacggctaa ttatgctta acttaggaag 300
agataaggca agagctagat tttttcatg tgatctttc caagcttcaa cttaacttaa 360
ctacatttct ctgtatgatg atgtcttta cttctacagg ttccttgagc ac 412

<210> 111
<211> 514
<212> DNA
<213> Homo Sapiens

<400> 111
taaattcaca tgcagtctca gagactatTTT agacaaagtT caagtttagga gcttttagga 60
tgtggagta aaactttat gggagggag ggctggctgc tggagaagg aagaagccag 120
actggttaga cagtagtctt aactccttagc ccagcctacg tgccctgccc ctctggccac 180
tgctgcagac acctgcctta acacacacac ctcttagact ccacagttt gccttaaagg 240
acctcccaa gtctccctt ccctgtctgg cttctccctt aagaagagag agataacttgt 300
agaattgggt gggggaaatg agcatgaact gtcctccat ttggatatg ttacattaga 360
gtgagagaga gaataaggag ctttcttat ggaagaaatg ggagaagaga gacagggttc 420
tttcagcag agtctatTTT tttctctgtt aggccaaata atctaaaaag actaacctgc 480
ccacccactc cttatattgc tgtgagattt cccc 514

<210> 112
<211> 489
<212> DNA
<213> Homo Sapiens

<400> 112
cgacccatc caagtcatct gattgaagag catgacagaa acaaaatgtt ttcaccaagc 60
atTTTtagat ttgactttt cactaaccag ttgacgagca gtgcatttac aaggcactgc 120
caaacaagat gcccgggaa gctgtgggg aaagaggacc tgccggctta gatcatctc 180
aattcctttt catgcctcc tgcattgtt ctgcgtgggt atttgtctcc ttagccatca 240
ggtagctttt acactacaat gtaagctata ggtggagcat cagcagttag tgaggccatt 300
cttcatcctt agatgtggc aatgaaatgtt tggtcaagt tccttctct tttgtgaatc 360
tttccccca tttctgttt acatgttaacc caacaaatgtt caatttctgt tgccctgtt 420
ccaatcagtt cttccctctg agtgagacgt acttggctac agatttctgc cttgtttgc 480
gacattgtc 489

<210> 113
<211> 416
<212> DNA
<213> Homo Sapiens

<400> 113		
gattggatgt gccttagctc ttagccaaac accttcctga caccatgagg gccagcagct	60	
tcttgcgtgt ggtgggttgc ctcatcgctg ggacgctgg tctagaggca gctgtcacgg	120	
gagttcctgt taaaaggtaa gacactgtca aaggccgtgt tccattcaat ggacaagatc	180	
ccgttaaagg acaagttca gttaaaggta aagataaaagt caaagcgcaa gagccagtca	240	
aaggccagt ctccactaag cctggctctt gccccattat ctgtatccgg tgccatgt	300	
tgaatcccc taaccgctgc ttgaaagata ctgactgccc aggaatcaag aagtgttg	360	
aaggctttt cgggatggcc tgtttcgttc cccagtgaag ggagccggtc ctgtct	416	
<210> 114		
<211> 502		
<212> DNA		
<213> Homo Sapiens		
<400> 114		
cccgaccgggt gggcatttgt gaggcccatg gttgagaaat gaataatttc ccaatttagga	60	
agtgttaagca gctgagggtct cttgagggag cttagccaat gtgggagcag cggtttgggg	120	
agcagagaca ctaacgactt cagggcaggg ctctgatatt ccatgaatgt atcaggaaat	180	
atatatgtgt gtgtatgttt gcacacttgt tttgtggct gtgagtgtaa gtgtgagtaa	240	
gagctgggtgt ctgattgtta agtctaaata tttccttaaa ctgtgtggac tgtatgcca	300	
cacagagtgg tctttctgga gaggttatag gtcactctg gggcctttt ggccccac	360	
gtgacagtgc ctggaatgt acttattctg cagcatgacc tgtgaccagc actgtctcag	420	
tttcaacttc acatagatgt ccctttctt gccagttatc cttttttt agcctagttc	480	
atccaaatcct cactgggtgg gg	502	
<210> 115		
<211> 430		
<212> DNA		
<213> Homo Sapiens		
<400> 115		
accacaacga cattgccttgc ctgaagatcc gttccaaggaa gggcaggtgt ggcgcacccat	60	
cccgactat acagaccatc tgcctgcctt cgtgtataa cgatccccag tttggcacaa	120	
gctgtgagat cactggctttt ggaaaagaga attctaccga ctatctctat ccggagcagc	180	
tgaagatgac tttgtgttttcc accgggatgt tcagcagccc cactactacg	240	
gctctgaagt caccacaaaa atgctgtgttgc ctgtgtatcc acagtgaaaa acagattcct	300	
gccagggaga ctcagggggaa cccctcgctt gttcccttcca aggccgcattt acttttactg	360	
gaattgtgag ctggggccgtt ggatgtgccc tgaaggacaa gccaggcgatc tacacgagag	420	
tctcacactt	430	
<210> 116		
<211> 449		
<212> DNA		
<213> Homo Sapiens		
<400> 116		
gggttgccat ccaagtggaaa gtcttttctt tgaccaaggg ggacagtcag ttttgcaaaa	60	

ggactcta at acctgttta a tattgtcttc ctaattggga taatttaatt aacaagat	120
actagaagtg aaactgcaac actaacttcc ccgtgctgtg gtgtgacctg agttggtgac	180
acaggccaca gaccccagag ctggctttt gaaacacaac tcaggcctt tgtgaaggtt	240
cccccgctga gatcttccct cctggttact gtgaagcctg ttggtttgc gctgtcgctt	300
ttgaggaggg cccatgggg taggagcagt tgaacctggg aacaaacctc acttgagctg	360
tgccttagaca atgtgaattc ctgtgttgct aacagaagtg gcctgtaagc tcctgtgctc	420
cggagggaaag catttcctgg taggctttt	449

<210> 117
<211> 535
<212> DNA
<213> Homo Sapiens

<400> 117 gctgaaggca gatgtcgcc caaagacagc tgagaacttc agagccctgt gcactggta	60
gaaggccttc ggctacaaag gctccaccc ttccacgggtg atcccttc tcatgtgc	120
ggcgggcgac ttcaccaacc acaatggcac aggccggaaag tccatctacg gaagccgctt	180
tcctgacgag aactttacac tgaaggcacgt gggccaggt gtcctgtcca tggcta	240
tggctctaacc accaacggct cccagtttccatctgcacc ataaagacag actggttgga	300
tggcaagcat gttgtgttcg gtcacgtcaa agagggcatg gacgtcgta agaaaataga	360
atcttcggc tctaagagtgggacatc caagaagatt gtcatcacag actgtggca	420
gttgagctaa tctgtggcca gggctgttgc atggggcag ctgcaaatgt ccatgcaccc	480
agggtggccgc gttggctgt cagccaaagg gcctgaaacg atacgtgtgc ccact	535

<210> 118
<211> 484
<212> DNA
<213> Homo Sapiens

<400> 118 ggttgaatgt ttgtccttag gataggccta tgtgttagcc cacaagaat attgtctcat	60
tagcctgaat gtgccataag actgaccctt taaaatgttt tgagggatct gtggatgctt	120
cgttaatttgc ttcagccaca atttatttgcgaaaatattct gtgtcaagca ctgtgggttt	180
taatattttt aatcaaacg ctgattacag ataatagtat ttatataaat aattaaaaaa	240
aattttctttt tggaaagagg gagaaaatga aataaatatc attaaagata actcaggaga	300
atcttcttta caattttacg tttagaatgt ttaaggtaa gaaagaaaata gtcaatatgc	360
ttgtataaaa cactgttcac tttttttttt aaaaaaaaaa cttgatttgtt tattaacatt	420
gatctgctga caaaacctgg gaatttgggt tgtgtatgcg aatgtttcag tgcctcagac	480
aaat	484

<210> 119
<211> 495
<212> DNA
<213> Homo Sapiens

<400> 119

42

gaacaagcgt	cctggggcat	ttgctattta	cctggaggct	tggcatttag	acatcttga	60
atcccttgc	ttaaagaaga	acacaggaaa	ggaagagcag	cgtgccagag	atctttctt	120
tgctcttgg	atccggatc	tcttcatgaa	acgagtggag	actaatcagg	actggtctt	180
gatgtgtcca	aatgagtgtc	ctggtctgga	tgaggttgg	ggagaggaat	ttgagaaact	240
atatgcaagt	tatgagaaac	aaggtcgtgt	ccgcaaagtt	gtaaaagctc	agcagcttg	300
gtatgccatc	attgagtctc	agacggaaac	aggcaccccg	tatatgctct	acaaagattc	360
ctgtaatcga	aagagcaacc	agcagaacct	gggaaccatc	aatatgcagca	acctgtgcac	420
agaaaatagt	gagtagcacca	gcaaagatga	ggttgtgtt	tgtatattgg	cttccctggc	480
cctgaatatg	tatgt					495

<210> 120

<211> 438

<212> DNA

<213> Homo Sapiens

<400> 120

gcccctggag	tcgcggagaa	agggccgtaa	ccggaggacc	cacgccccctg	agcctcgccc	60
tgagcggggg	ccgcgcagcg	caacgcactg	gtgaccagac	tgtccccacg	ccgggaacca	120
agcaggagac	gacaggcgag	agaggagcca	gacagaccct	gaaaagaagg	acgggttggg	180
gccgggcaca	ttgggggtca	ccggccgtat	gagacaccaa	ccgacaggcc	ctggctgagg	240
gcagctgcgc	gggcttattt	attaacagga	taacccttga	atgttagcagc	ccccggaggg	300
cggcacaggt	cgggcgcagg	attcagccgg	agggaaaggga	cggggaagcc	gagctccaga	360
gcaacgacca	gggcccggagga	ggtgcctgga	gtgcccaccc	tgggagacag	accccaccc	420
cttgggtagt	gagcagtg					438

<210> 121

<211> 447

<212> DNA

<213> Homo Sapiens

<220>

<221> misc_feature

<222> (116)..(116)

<223> n is a, c, g, or t

<220>

<221> misc_feature

<222> (362)..(362)

<223> n is a, c, g, or t

<400> 121

ggaactacgg	ggcttacagg	agcttttgt	tgcctggtag	aaactatttc	tgttccagtc	60
acattgccat	cactttgtt	ctgcctgcca	ccggggagga	ggctggtagc	aggccnaaag	120
gccagtggaa	gaaacaccct	ttcatctcag	agtccactgt	ggcactggcc	acccctcccc	180
agtacagggg	tgctgcaggt	ggcagagtga	atgtccccc	tcatgtggcc	caactctcct	240
ggcctggcca	tctccctccc	cagaaacagt	gtgcattgggt	tatttggag	tgttaggtgac	300
ttgtttactc	attgaagcag	atttctgtt	ccttttattt	ttataggaat	agaggaagaa	360
angtcagatg	cgtgcccagc	tcttcacccc	ccaatctt	ggtggggagg	ggtgtacct	420

aatatttatac atatccttgc ccttgag	447
<210> 122	
<211> 323	
<212> DNA	
<213> Homo Sapiens	
<400> 122	
aaatttgacca tacaatttca tcctccttca ggggatcaaa aggacggagt ggggggacag	60
agactcagat gaggacagag tggtttccaa tgtgtcaat agattttagga gcagaaaatgc	120
aaggggctgc atgacacctacc aggacagaac tttcccaat tacagggtga ctcacagccg	180
cattggtgac tcacttcaat gtgtcatttc cggtcgctgt gtgtgagcag tggacacgtg	240
aggggggggt gggtgagaga gacaggcage tcggattcaa ctaccttaga taatatttct	300
gaaaacctac cagccagagg gta	323
<210> 123	
<211> 499	
<212> DNA	
<213> Homo Sapiens	
<400> 123	
gtatcaggct tcaattccat tatgtttaa tgggtctct gaagatgact tgtgatttt	60
ttttttttt tttaaaccat gaagagccgt ttgacagagc atgctctgcg ttgttggtt	120
caccagcttc tgccctcaca tgcacagggta tttaacaaca aaaatataac tacaacttcc	180
ctttagtct cttatataag tagagtccctt ggtactctgc cctcctgtca gtagtggcag	240
gatctattgg catattcggg agcttcttag agggatgagg ttcttgaac acagtgaaaa	300
tttaaattag taactttttt gcaaggcagtt tattgactgt tattgctaag aagaagtaag	360
aaagaaaaag cctgttggca atcttggta tttcttaag atttctggca gtgtggatg	420
gatgaatgaa gtggaatgtg aactttggc aagttaaatg ggacagcctt ccatgttcat	480
ttgtctacct cttaactga	499
<210> 124	
<211> 328	
<212> DNA	
<213> Homo Sapiens	
<400> 124	
taattttaga ttgcgccttac aatgtaaatc ttcacattgg agataatatt gggtggacct	60
tgcctatctt cactctagcc ttctgtatgg tgaaggactc agccaccccttc cttcttacc	120
ccatgcttct caccaaattt ttgttgtcat tgaggcact tggataactc aagttgatata	180
ttatagctga tcaatctata tgtgtcacag aactatgctg cctaaagtga tcttggctcc	240
ttaatggtcc ttttggcccc ttggatagtt aacagctgag taattctaat ctcttctgtg	300
ttttccttgc cttaaccaca aattgtgg	328
<210> 125	
<211> 489	
<212> DNA	
<213> Homo Sapiens	

<400> 125
gagatacaga acttggtgac ccatgtattg cataagctaa agcaacacag acactcctag 60
gcaaagttt tgtttgtgaa tagtacttgc aaaacttcta aatttagcaga tgacttttt 120
ccatgtttt ctccagagag aatgtgctat atttttgtat atacaataat atttgcaact 180
gtaaaaaca agttgtgcca tactacatgg cacagacaca aaatattata ctaatatgtt 240
gtacattcgg aagaatgtga atcaatcagt atgttttag attgtatTTT gccttacaga 300
aagccttat tgtaagactc tgatTTCCt ttggacttca tttatTTTt acagttacag 360
taaaattcaa cctttatTTT ctaatTTTt caacatattg ttttagtgtaa agaatattt 420
tttgaagttt tattatTTTt taaaaaagaa tatttatttt aagaggcatc ttacaaattt 480
tgccccTTT 489

<210> 126
<211> 503
<212> DNA
<213> Homo Sapiens
<400> 126
gcggcatgtg accatcattg aactggggg acagccacct caggagggtgg ggcgcaccc 60
ggagcaacag ctgtcagcca acatcatcgaa ggagtcagg caatttcagc gcctcactcg 120
ctcctacttc aacatgggtt tgattgacaa gcagggtatt gaccgagacc gctacatgg 180
acctgtcacc cccgaggaaa tcttcacatt cattgatgac tacctactga gcaatcagga 240
gttgaccagg cgtcggggc aaagggacat atgcgagtga acttgagcca gggcatgg 300
aaagtcaagg gaaaagctcc tctagttgc tggaaactggg acctaataaa aggaggaaat 360
gtttcccac agttcttaggg acaggactct gaggtgggtg agtttgacaa atcctgcagt 420
gtttccaggc atcTTTTTt gactgtgtaa tagttccctt agaagctagg tagggactga 480
ggacaggcct tggggcagtgg gtt 503

<210> 127
<211> 436
<212> DNA
<213> Homo Sapiens
<400> 127
agactggcgcg aaaggctgtc cggagggcag accaggtgcc ttgcgcaga gaaaacacca 60
aagtctcctg ttgcgtcata aagaagtttt tggatgggaa gagaatccag accatcttgg 120
ggcagccagg cccttgcctt cattttaca gaggtgcac aactgattcc aacacaaaac 180
cccttccctt tttaaaatg atttctgttc taatgccata gatcaaaggc ctcagaaacc 240
attgtgtttt tcctctttga agcaatgaca agcactttac tttcacgggtg gttttgttt 300
tttcttattt ctgtggacc tctttggag gacgttaaag gcgtgttttta cttgttttt 360
taagagtgtg tgatgtgtgt ttttagatt tcttgacagt gctgtaaatac agacggcaat 420
gcaatagcct attaa 436

<210> 128
<211> 497
<212> DNA
<213> Homo Sapiens

<400> 128
cctgccctct agttggttct gggcttgcat ctctccaaac ctgcccagtc acagaaggag 60
gaatgactca aatgccccaaa accaagaaca cattgcagaa gtaagacaaa catgtatatt 120
tttaaatgtt ctaacataag acctgttctc tctagccatt gatttaccag gctttctgaa 180
agatcttagt gttcacacag agagagagag agtactgaaa aagcaactcc tcttcttagt 240
cttaataatt tactaaaatg gtcaactttt cattatcttt attataataa acctgatgct 300
ttttttaga actccttact ctgatgtctg tataatgtgc actgaaaagg ttaatattta 360
atgttttaat ttatitgtg tggtaagttt attttgattt ctgtaatgtg ttaatgtgat 420
tagcagttat tttccttaat atctgaatta tactaaaaga gtatgtgacatataagacg 480
caatttgtt tttcagt 497

<210> 129
<211> 321
<212> DNA
<213> Homo Sapiens

<400> 129
gttggatgg tggaaaggctc cattttattt agattttaa gatacatgca aaggtttgg 60
aatagaacct ctggcaccc tcctcagtgt gggggctg agagttaaag acagtgtggc 120
tgcagtagca tagaggcgcc tagaaattcc acttgcaccc tagggcatgc tgataccatc 180
ccaatagctg ttgcccattt acctcttagt gtgagttct agaatactgg tccattcatg 240
agatattcaa gattcaagag tatttcact tctgggttat cagcataaac tggaatgtag 300
tgtcagagga tactgtggct t 321

<210> 130
<211> 553
<212> DNA
<213> Homo Sapiens

<400> 130
tttgccgtca gtttcttgc tagatttgaa aattgtatac caatgtgttt tctgttagact 60
ctaagataca ctgcactttt ttttagaaaaaa aaactgaaga tggaaatataat attgtaaaga 120
agggatatta agaatcttag ataacttctt gaaaaagatg gcttatgtca tcaatgtttt 180
acctttatgt tatgaggata taatgtgtgc tttattgtat tagaaaattt gtgaccatata 240
ttcacaggtg gacaaatgtt gtcctgttaa tttataggag tttttgggg atgtggaggt 300
agttggtag aaaaattttaa agaacattca ctttgcattttt cagttttttt cttttttttt 360
gttatataatgtt ggatgtatata cacagtggca aaacaaaaatgtt acattgtttttaa aaatataatgtt 420
tggaaaaatgtt cactatatct tcccaattttt cattgtttttt gtatattggg tttttttttt 480
tgacatcaaa acttggaccc ttggaaaaca aaagttttaa ttaaaaaaaaa tccttgcac 540
ttacaatttttgcac 553

<210> 131
<211> 419
<212> DNA
<213> Homo Sapiens

<400> 131
gagtcggaga tcatgcacca cacacacaat tccccagccc agtgatgtt gtgttgcacca 60
gatgttcctg agtctggagc aagcacccag gccagaataa cagagcttc ttagttggtg 120
aagacttaaa catctgcctg aggtcaggag gcaatttgcc tgccttgcacaaaagctcag 180
gtgaaagact gagatgaatg tcttcctct ccctgcctcc caccagactt ctcctggaa 240
aacgctttgg tagatttggc caggagctt ctatgtt aattggataa atacacacac 300
catacactat ccacagatat agccaagtag atttggtag aggatactat ttccagaata 360
gtgttagct cacctagggg gatatgttg tatacacatt tgcataacc cacaatgggg 419

<210> 132
<211> 414
<212> DNA
<213> Homo Sapiens

<400> 132
tttgtgtcggt tgctgtttt aagaaaatca tgacattcca agttgacatt ttttttttca 60
ttttattaa aatttggaaat tctgaacacc gtcagcaccc tctcttcctt atcatgggtc 120
atctgacccc tgtccgtctc ctgtccctg ctcatgttt gggggcctt ctttaactgc 180
cttcctggct tagctcagat ggcagatgag agttagtca agggcctggg cacaggaggg 240
agagctgcag agtgcctgc ctgccttggc tggagggaca cctctcctgg gtgtggagac 300
agcttgggttc ctttcctcta gtcctctggt gggtaatgc cacctcctga gatcctcacc 360
tcttggatt aaaattgttg gtcactgggg aaaggctgag tttgcaacca gttt 414

<210> 133
<211> 419
<212> DNA
<213> Homo Sapiens

<400> 133
agggctgaa ctatcggtat cacctgggtt gtaactgcaa gatcaagtcc tgctactacc 60
tgcccttgcctt tggacttcc aagaacgagt gtctctggac cgacatgctc tccaatttcg 120
gttaccctgg ctaccagtcc aaacactacg cctgcattccg gcagaaggcc ggctactgca 180
gctggtaccg aggatggcc ccccccggata aaagcatcat caatgccaca gaccctgag 240
cgccagaccc tgccccaccc cacttcctc cttccctgct gagttccct tggacactaa 300
ctcttccctgg atgatgacaa tggaaatttttgc tggccaaattt agcactttgg 360
acattnaaag aaaggcttat gtcacttgc ggggttatt gggactatc ctccctggcc 419

<210> 134
<211> 493
<212> DNA
<213> Homo Sapiens

<400> 134
gacttttgg aatagccctg tctaggccaa actgtggccc ccaggagaca ctacccttcc 60
atgccccaga cctctgttgc gcatgtgaca attgacaatc tggactaccc caagatggca 120
cccaagtgtt tggcttctgg ctacctaagg ttaacatgtc actagagtat tttatgaga 180
gacaaacatt ataaaaatct gatggcaaaa gcaaaacaaa atggaaagta ggggaggtgg 240

47

atgtgacaac aacttccaaa ttggctctt ggaggcgaga ggaaggggag aacttggaga	300
atagttttg ctttgggggt agaggctct tagattctcc cagcatccgc ctcccctt	360
agccagtctg ctgtcctgaa acccagaagt gatggagaga aaccaacaag agatctcgaa	420
ccctgtctag aaggaatgta tttgttgcta aatttcgttag cactgtttac agtttcctc	480
catgttattt atg	493

<210> 135
<211> 567
<212> DNA
<213> Homo Sapiens

<400> 135 gagtattact agagcttgc cacctctcca ttttgcctt ggtgctcatc ttaatggcct	60
aatgcacccc caaacatgga aatatcacca aaaaatactt aatagtccac caaaaggcaa	120
gactgccctt agaaattcta gcctggttg gagatactaa ctgctctcag agaaagttagc	180
tttgcacat gtcatgaacc catgtttgca atcaaagatg ataaaataga ttcttatttt	240
tcccccaccc ccgaaaatgt tcaataatgt cccatgtaaa acctgctaca aatggcagct	300
tatacatagc aatggtaaaa tcatcatctg gatttaggaa ttgctttgt cataccccc	360
agttctaaag atttaagatt ctccctacta ctatcctacg tttaaatatc ttgaaagtt	420
tgtattaaat gtgaatttta agaaataata tttatatttc tgtaatgta aactgtgaag	480
atagttataaa actgaagcag atacctggaa ccacctaag aacttccatt tatggaggat	540
tttttgcctt cttgtgtttg gaattat	567

<210> 136
<211> 479
<212> DNA
<213> Homo Sapiens

<220> <221> misc_feature <222> (441)..(441) <223> n is a, c, g, or t	
<400> 136 accaagggttc tcatgaatct ccaaccttaa atcctgaaac agtggcaata aatttatctg	60
atgttgactt gagtaaatat atcaccacta ttgctggagt catgacacta agtcaagtt	120
aaggctttgt tcgaaagaat ggtgtcaatg aagccaaaat agatgagatc aagaatgaca	180
atgtccaaga cacagcagaa cagaaaggta aactgcttcg taattggcat caacttc	240
gaaagaaaaga agcgtatgac acattgatta aagatctcaa aaaagccaaat ctttgtactc	300
ttgcagagaa aattcagact atcatcctca aggacattac tagtgcactca gaaaattcaa	360
acttcagaaa tgaaatccaa agcttggct agagtgaaaa acaacaaatt cagttctgag	420
tatatgcaat tagtgtttga naagattctt aatagctggc tgtaatact gcttggttt	479

<210> 137
<211> 490
<212> DNA
<213> Homo Sapiens

```

<400> 137
gtacgagctc acataactgg gaccagagga agaagcaaca cattgtcttc tccaaactcc      60
aagaatgaaa aggctctggg ccgcaaata aactcctggg aatcatcaag gagtgggcat      120
tcattcctga gcaacttgca cttgagaaat ggtgaactgg tcatccatga aaaagggtt      180
tactacatct atccccaaac atactttcgta ttccaggagg aaataaaaaga aaacacaaag      240
aacgacaaac aaatggtcca atatattac aaatacacaa gttatcctga ccctataattg      300
ttgatgaaaa gtgctagaaa tagttgtgg tctaaagatg cagaatatgg actctattcc      360
atctatcaag gggaatatt tgagcttaag gaaaatgaca gaattttgt ttctgtaaca      420
aatgagcaact tgatagacat ggaccatgaa gccagtttt tcggggcctt ttttagttgc      480
taactgacct                                         490

<210> 138
<211> 248
<212> DNA
<213> Homo Sapiens

<400> 138
ctctaccta tatcagtttg cttagcagaaa tctagaagac tgtcagcttc caaacattaa      60
tgcaatggtt aacatcttct gtctttataa tctactcctt gtaaagactg tagaagaaag      120
cgcaacaatc catctctcaa gtatgtatc acagtagtag cctccaggtt tccttaaggg      180
acaacatcct taagtcaaaa gagagaagag gcaccactaa aagatcgtag tttgcctggt      240
gcagtggc                                         248

<210> 139
<211> 405
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (64)..(64)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (68)..(68)
<223> n is a, c, g, or t

<400> 139
gctcacccag cagatgttcg atgccaagaa catgatggcc gcctgcgacc cgccacgg      60
ccgntanct gacggtggcc accgtgttcc gggccgcat gtccatgaag gaggtggacg      120
agcagatgct gccatccag agcaagaaca gcagactt cgtggagtgg atccccaaaca      180
acgtgaaggt gccgtgtgt gacatccccgc cccgcggcct caagatgtcc tccacctca      240
tcgggaacag cacggccatc caggagctgt tcaagcgcat ctccgagcag ttcacggcca      300
tgttccggcg caaggccttc ctgcactgtt acacgggcga gggcatggac gagatggagt      360
tcaccgaggc cgagagcaac atgaacgacc tggtgtccga gtacc                         405

<210> 140
<211> 407
<212> DNA

```

<213> Homo Sapiens

<400> 140
 gatgcctaac caaggactag agtccttct tgagatctaa atctaaagta aatgtgcatt 60
 aaagcagtgt gcttcaaagg catcacgacga taaaagcaac ataccacaac taggagttat 120
 ttctcaaact taaaatgtcct ctggaaatcc agactaaaaa ataagagcaa acttaacaca 180
 ctatccattt tcgagcaaac ttaaccoact atatccattt tgctcatgtg ttttatgcaa 240
 ccagcttcc atcaaattcct caatccttga atccaggtaa aaggtaattt atcctaggat 300
 tagtgaatga ttcaatgaag ctttcttcaa aacaaacata ggagtgtaat gtactattat 360
 gtttgatcc tgtttagtt tataaagcac tttcacatac attatgg 407

<210> 141

<211> 518

<212> DNA

<213> Homo Sapiens

<400> 141
 acccaactac tctggtagcca ttgccttggc cctgttagtg tcgccttgg gaggtttgc 60
 ttatggaga aggaacaact tggagttcat ctataacaag actgggttggg ccatggtgcc 120
 tctgtgtata gtctttgcta tgacttctgg ccagatgtgg aaccatatcc gtggaccc 180
 atatgctcat aagaacccac acaatggaca agttagctac attcatggga gcagccaggc 240
 tcagtttgtg gcagaatcac acattattct ggtactgaat gccgctatca ccatggggat 300
 ggttcttcta aatgaagcag caacttcgaa aggcatgtt ggaaaaagac ggataatttg 360
 cctagtgaaa ttgggcctgg tggcttctt ctcaagtttt ctactttcaa tatttcgttc 420
 caagtaccac ggctatcctt atagtgtatc ggacttttag tgagaagatg tgatttgac 480
 catggcactt aaaaactcta taacctcagc ctttaat 518

<210> 142

<211> 443

<212> DNA

<213> Homo Sapiens

<400> 142
 ctttgctatg acttctggcc agatgtggaa ccataccgt ggacccat atgctataa 60
 gaacccacac aatggacaag tgagctacat tcatggagc agccaggctc agtttgtggc 120
 agaatcacac attattctgg tactgaatgc cgctatcacc atggggatgg ttcttctaaa 180
 tgaagcagca acttcgaaag gcgatgtgg aaaaagacgg ataatttgcc tagtgggatt 240
 gggcctggtg gtcttcttct tcaagttttctt actttcaata tttcgatccaa agtaccacgg 300
 ctatccttat agcttttaa taaaatgaag ccaagtgaaa ttgcataaa gtgaatgttt 360
 accatgaaga taaaactgttc ctgactttat actatttga attcattcat ttcattgtga 420
 tcagctagct tattttgtg tac 443